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DEFINING AND MEASURING SUSPICION OF SEPSIS

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ABSTRACT

OBJECTIVES

To define the target population of patients who have suspicion of sepsis and to provide a basis for assessing the burden of suspicion of sepsis; and the evaluation of sepsis guidelines and improvement programmes.

DESIGN

Retrospective analysis of routinely collected hospital administrative data.

SETTING

Secondary care, eight NHS Acute Trusts.

PARTICIPANTS

Hospital Episode Statistics data for 2013-2014 was used to identify all admissions with a primary diagnosis listed in the "suspicion of sepsis" coding set. The suspicion of sepsis coding set consists of all bacterial infective diagnoses.

RESULTS

We identified 54774 admissions with suspicion of sepsis, equivalent to a rate of 22 admissions per 1000 adults in a given year. The mortality for this group was 6.3% during their acute hospital admission. Urinary tract infection was the most common diagnosis and lobar pneumonia was associated with the most deaths. A short list of ten diagnoses can account for over 85% of the deaths.

CONCLUSIONS

Patients with suspicion of sepsis can be identified in routine administrative data. It is these patients who should be screened for sepsis and are the target of programmes to improve the detection and treatment of sepsis. The effectiveness of such programmes can be evaluated by examining the outcomes of patients with suspicion of sepsis.

KEY WORDS: sepsis, suspicion of sepsis, epidemiology, improvement programmes

STRENGTHS & LIMITATIONS OF THIS STUDY

- Our methodology for identifying suspicion of sepsis (SOS) uses routine administrative data, providing a means of assessing the SOS burden and comparing patient outcomes over time and across organisations.
- Monitoring the outcomes of SOS patients provides a simple and effective means of measuring the impact of sepsis improvement programmes.
- The analysis allowed the most common and the most high risk infections to be identified.
- The mortality figures are limited to in hospital deaths: 30 day mortality data was unavailable.
- The estimates for the SOS burden are based on Hospital Episode Statistics data which ultimately may not be as accurate as prospective data based on clinical and physiological measurements.

Sepsis, defined as a "life-threatening organ dysfunction caused by a dysregulated host response to infection",[1] is one of the leading causes of death.[2,3] The incidence of sepsis is thought to be increasing [4-7], with estimates of up to 300 cases per 100,000 population,[8] and it has been recently cited as the most expensive reason for hospitalisation in the US.[9] Rapid, evidence-based, aggressive treatment and assiduous review are vital for preserving post-recovery function and ensuring survival. Sepsis is most common in the elderly and those with impaired immune systems and is associated with reduced quality of life and high rates of late mortality in those who survive.[10,11]

Worldwide awareness of sepsis has been increasing due to high profile media attention, coupled with reports from the surviving sepsis campaign and a multitude of national regulators and expert bodies.[12-15] The early detection and treatment of sepsis has been highlighted as a major focus for improvement. For example, in the UK the identification and early treatment of sepsis is the target of a major national campaign and also the focus for Commissioning for Quality and Innovation (CQUIN) for 2015-2018, a financial incentive system.[16] The lack of suitable metrics for sepsis have hampered evaluation and some have suggested that until this is resolved no sepsis campaigns should be launched.[17]

Measures of the incidence of sepsis

There are three broad approaches to assessing the incidence of sepsis: through laboratory analytic tests such as blood cultures, through clinical judgement and through administrative databases (essentially the recording of clinical judgement). Many patients with sepsis do not have currently identifiable bacterial growth in blood tests (positive blood cultures), meaning that these investigations alone cannot assess the incidence of sepsis.[18,19] Clinical studies of sepsis have been primarily focused on intensive care units (ICUs) and suggest that the incidence of severe sepsis in intensive care is approximately 30%.[20,21] However, these studies, while informative in the intensive care environment, do not address the incidence of sepsis in other clinical settings within the hospital which is where most improvement programmes are now focused and where the majority of septic patients are managed.

The most practical means of assessing the incidence of sepsis in the wider hospital environment is through the analysis of administrative databases. However there is great variability in estimates of sepsis incidence depending on the coding set used [23,24] and changes in coding practices overtime make comparisons between years difficult.[17,22,24] In the UK,

clinicians rarely document "sepsis or septicaemia" in the admission documentation and tend to prioritise documenting the source of infection.[12,13] Official estimates for sepsis incidence, such as the Health Episode Statistic figures reported by NHS England, are broadly based on septicaemia codes,[5] and therefore underestimate the true incidence. Studies in the US frequently report rising sepsis incidence and falling mortality: it is unclear whether the falling mortality is due to actual improvements in care or a diluting effect of increased coding of patients who are less sick than those who would previously have been included.[25] In any case, the wider aim is not so much the treatment of sepsis as the prevention of sepsis through early intervention in patients who are at risk of sepsis.

Suspicion of sepsis

The concept of assessing and treating patients with suspected sepsis is central to the recently published National Institute for Health and Care Excellence (NICE) guidelines, with clinicians urged to think sepsis for all patients with signs of infection.[26,27] In practice clinicians do not wait to diagnose sepsis but rapidly treat patients with an infection that is serious enough to warrant hospital admission; they endeavour to intervene to prevent full blown sepsis developing and to interrupt the dangerous dysregulated and harmful immune response that may emerge. Some of these patients will of course already have a "bad or serious infection" that is sufficient to warrant the term sepsis. Most sepsis campaigns and improvement programmes do not actually target the treatment of fully developed sepsis but instead are aimed at the rapid detection and treatment of patients who have suspected sepsis when admitted to hospital from the community. This means that we must, first and foremost, identify those patients who either have early sepsis or who have an infection which might develop into sepsis if not properly treated.

The group, "suspicion of sepsis", consists primarily of patients who have a bacterial infection serious enough to require hospital admission.[28,29] Defining this group is essential to the implementation of NICE guidelines and to all the recommendations for research proposed in the guidelines.[26] Although there are non-bacterial causes of sepsis (e.g. viruses, protozoa), these are (generally) far less common and amenable to treatment. Given that the majority of septic patients have community-acquired infections,[30] our focus, and that of most sepsis improvement programmes, will be on patients with infections at the time of admission. To evaluate programmes aimed at early detection and intervention we must therefore define a "suspicion of sepsis" group and monitor the progress of its members. A successful

intervention would see a reduction in later sepsis (however measured) but even in the absence of reliable sepsis definition we could monitor mortality, length of stay and other indices of outcome in a suspicion of sepsis group.

Identifying patients with "suspicion of sepsis"

The primary aim of this study is to estimate the number of patients with suspicion of sepsis (SOS) on admission to hospital and their outcomes (mortality, length of stay, readmission rate). We focus on patients who either have bacterial infections which may lead to sepsis or which have already led to early sepsis. Analysis of a full list of ICD-10 diagnostic infection codes that can cause sepsis will provide clinical insight into which infections are the most frequent, which are the most dangerous and which might be prioritised for future improvement strategies. The full list of infection codes will inevitably include many rare or unusual diagnoses which would not be useful in assessing routine local activity or the impact of sepsis improvement programme. A secondary aim is therefore to propose a short pragmatic set of codes which can be used as a key aspect of a measurement suite for tracking the progress of sepsis improvement efforts in the UK.

METHOD

A list of International Statistical Classification of Diseases and Related Health Problems Tenth Revision (ICD-10: 2015) codes was developed for infective bacterial pathogens that can cause sepsis (see Appendix A). The coding set entitled "Suspicion of Sepsis" was established on the basis of clinical consensus: a consultant in acute medicine (MIK) reviewed the full list of ICD-10 codes and identified all codes known to be infective bacterial pathogens, requiring treatment with antibiotics. Specialist consultants for each organ system were then asked to verify the list of codes relevant to their speciality and the codes were subsequently adjusted based on their feedback. The list also includes specific sepsis codes (A40/A41) which are commonly used in the UK for instances of sepsis where the source of infection is unknown.[12 13]

Hospital Episode Statistics (HES) data was obtained for all acute trusts in the Oxford Academic Health Science Network (AHSN) region (n=8) for the financial year 2013-14: the region covers a population of 3.3 million. The data originated from the Health and Social

Care Information Centre (HSCIC). A data warehouse was created in Microsoft SQL Server for running queries and completing data analysis.

We analysed the admission episode to determine if any of the ICD-10 "Suspicion of Sepsis" codes appeared as the primary diagnosis. Patients under the age of 18 were excluded. For each identified admission, the following information was determined: age at admission, sex, number of hospital deaths and associated mortality, length of stay (LOS) and readmission rate.[a] Population data provided by the Clinical Commissioning Groups (CCGs) which fall within the Oxford AHSN region was used to estimate a population incident rate.

Patient involvement

Patient experiences guided the principles of this study: a consistent theme in patient stories and local reviews of sepsis cases is that early symptoms were not recognised. Patients were not involved in the study design or the technical analysis of administrative databases. The concepts of the paper have been presented to both patients and carers in the context of measuring the impact of sepsis improvement programmes.

RESULTS

Incidence and demographics

In 2013-14, 54774 admissions were identified in the Oxford AHSN region using the "suspicion of sepsis" coding set, yielding a population estimate of 22 SOS hospital admissions per 1000 adults in a given year. The overall in-hospital mortality rate for this group was 6.3%, which represents 3452 deaths. The mean length of stay (LOS) was 6.4 days and the readmission rate was 6.2%.

The number of SOS admissions by age and gender and the mortality rate by age are shown in Figure 1. The patient was female in 53.4% of admissions. The number of admissions increased gradually with age, before decreasing for over 85s. Women between 18 and 35 (child-bearing age) were almost twice as likely as men of the same age to have suspected sepsis and women over 85 also had a higher incidence than men, likely as a result of the higher female population in comparison to men over 85 years. For all other age groups, the

[a] A patient was classified as a readmission if they were admitted as an emergency readmission between 1 and 30 days after their previous discharge. The main speciality of the two spells needed to match in order to be classified as a readmission.

number of SOS admissions in men and women were similar. Hospital mortality increased with age. The mortality rate was less than 1% for all age groups up to aged 45. From 46 upwards, the mortality increased exponentially: for patients over 85, the mortality was 18.1%.

Most common diagnoses

The following four ICD-10 chapters combined account for over 85% of SOS admissions: "Diseases of the Respiratory System" (34.3%), "Diseases of the Digestive System" (22.8%), "Diseases of Genitourinary System" (18.1%) and "Diseases of Skin and Subcutaneous Tissue" (10.8%). 2577 (4.7%) of the SOS admissions had a septicaemia code (A40/A41) as their primary diagnosis.

Table 1 lists the twenty five most common diagnoses, alongside their respective mortality rates, number of deaths, LOS and readmission rates. A complete list of all the suspicion of sepsis diagnoses with the number of admissions, number of deaths, mortality, length of stay, and readmission rate is presented in Appendix B. The majority of the diagnoses in Table 1 are infections of the respiratory system. The most common diagnosis was urinary tract infection. A419 sepsis, the most common of the septicaemia codes was the eighth most common SOS diagnosis.

The secondary aim of this study was to develop a short set of codes which could be easily tracked. The 25 diagnoses in Table 1 capture 80.5% of the total number of SOS admissions and 85.9% of the deaths. These 25 diagnoses include a number of diagnoses which are common but rarely lead to poor outcomes.

Diagnoses associated with the most deaths

The most important patients to identify and track in improvement programmes are those who have the poorest outcomes. Table 2 lists the ten diagnoses associated with the most deaths. Lobar pneumonia was associated with the most deaths, followed by pneumonia unspecified and then urinary tract infection. A419 sepsis was fourth on the list. Respiratory infections featured frequently in Table 1: indeed diagnoses from the ICD-10 chapter "Diseases of the Respiratory System" accounted for 69.2% of the total number of SOS deaths.

Together the ten diagnoses listed in Table 2 account for 86.7% of the total number of SOS deaths and 50.2% of the total number of SOS admissions. The mortality for this group of ten diagnoses is 10.6%, the mean LOS is 9.6 days and the readmission rate is 7.3%: these are

much poorer outcomes than for the 25 more common diagnoses where the mortality is 6.7%, the mean LOS is 4.7 days and the mean readmission rate is 5.9%. Figure 2 shows a visual representation of these ten high risk diagnoses, their frequency, their outcomes (mortality and length of stay) and the type of infection. Early intervention and treatment improvement programmes should aim to improve the outcomes for patients admitted to hospital with these ten diagnoses.

DISCUSSION

Our methodology identifies those patients who should be routinely screened for sepsis on admission to hospital. Based on the identification of 54,774 suspicion of sepsis admissions in Oxford AHSN region in the financial year 2013-14, we estimate 22 SOS hospital admissions in a population of 1000 adults in a given year. Analysis of the individual SOS diagnoses allows a short pragmatic set of codes to be developed. For instance, the top ten diagnoses associated with the highest numbers of hospital deaths can account for over 85% of the total number of SOS deaths: monitoring the outcomes of patients admitted to hospital with one of these ten crucial diagnoses, (e.g. mortality, length of stay, readmission rate), would be a pragmatic and effective means of assessing sepsis campaigns and improvement efforts.

Previous studies have found that the number of recorded septic episodes has artificially increased as a result of increased coding rather than solely more cases of sepsis, particularly in the US.[24] By tracking infective diagnoses, our methodology avoids this bias and hence would be a more effective measure of improvement over longer time periods. Clinical specialities are also more easily able to identify and track patients who are particularly relevant to them. Different countries could also use the methodology from this study to identify the most common and most fatal suspicion of sepsis diagnoses in their countries. The full suspicion of sepsis coding set could also be used to compare figures internationally for the population with suspicion of sepsis.

Future research and evaluation

We have been able to estimate the size of the suspicion of sepsis population on admission to hospital in our region; this should now be done nationally. Ideally we would also want to measure the percentage of SOS cases who develop definite sepsis, which would mean we would have a means of evaluating campaigns and programmes which aim to improve the

detection and early treatment of potential sepsis. However, major improvements are needed in the quality of coding of sepsis if we are to use ICD codes to identify definite cases of sepsis. Even if we used case note review, evidence shows that diagnosing sepsis is subjective and variable.[31] The exact size of the sepsis "bubble" within the SOS set is likely to remain unknown in the absence of a definitive diagnostic test. However, linking the SOS database with electronic clinical observation data (e.g. physiology and pathology blood results) may allow specific definitions of sepsis to be applied. A potential surrogate measure may be the proportion of SOS patients admitted to intensive care.

Future studies can use the suspicion of sepsis population to study predictors of poor outcomes, for example by linking the SOS database with electronic clinical observation data. Suspicion of sepsis could also be used to assess the usefulness of potential biomarkers and to assess the impact of improvement campaigns, from small scale quality improvement work to national strategies such as the new NICE guidelines. Future studies should also estimate the costs and associated bed days for suspicion of sepsis.

Limitations

Our mortality figures are based on Hospital Episode Statistics data and are therefore limited to in hospital deaths: future studies should also endeavour to assess 30 day mortality. Secondly, our estimates for the size of the SOS population are based on ICD codes which ultimately may not be as accurate as prospective data based on clinical and physiological measurements. However, our approach can be easily and cheaply used by any organisation to identify and monitor this critical group of patients. It is also worth noting that our estimates are based on one area of the country. Variability between regions is likely to be affected by such factors as social economic conditions, the quality of the hospitals and the average age of the population. Our figures for the population incidence with suspicion of sepsis do suggest however that the national burden is substantial.

Conclusions

We propose that patients admitted to hospital for infection ("Suspicion of Sepsis") are a critical target population both for screening for sepsis and for monitoring the impact of sepsis improvement efforts. This group can be easily identified from routine administrative data. Analysis of local UK data yields an estimate of 22 hospital admissions with suspicion of sepsis per 1000 adults in a given year and revealed that a short list of ten diagnoses can

capture over 85% of suspicion of sepsis deaths. Monitoring the outcomes of suspicion of sepsis patients is a simple and effective measurement strategy for evaluating programmes aiming to improve the detection and treatment of sepsis.

TABLES & CHARTS

Table 1: **Top 25 most common "Suspicion of Sepsis" diagnoses in Oxford AHSN region (2013-14)**

Diagnosis	No. of admissions	No. of deaths	Mortality (%)	LOS	Readmission (%)
1. N390 - Urinary tract infection, site not specified	7088	285	4.0	9.0	6.4
2. K573 - Diverticular disease of large intestine without perforation or abscess	5414	9	0.2	0.8	1.3
3. J181 - Lobar pneumonia, unspecified	5265	990	18.8	9.8	6.3
4. J22X - Unspecified acute lower respiratory infection	3808	167	4.4	6.5	7.4
5. J189 - Pneumonia, unspecified	3126	483	15.5	9.6	7.1
6. L031 - Cellulitis of other parts of limb	2983	62	2.1	6.9	7.5
7. J440 - Chronic obstructive pulmonary disease with acute lower respiratory infection	2854	184	6.4	7.2	11.3
8. A419 - Sepsis, unspecified	1882	280	14.9	9.2	10.7
9. K805 - Calculus of bile duct without cholangitis or cholecystitis	1167	2	0.2	1.7	7.6
10. T814 - Infection following a procedure, not elsewhere classified	1067	3	0.3	5.9	7.7
11. J039 - Acute tonsillitis, unspecified	1055	0	0.0	1.2	5.7
12. K358 - Acute appendicitis, other and unspecified	993	0	0.0	2.9	6.4
13. N12X - Tubulo-interstitial nephritis, not specified as acute or chronic	809	1	0.1	3.5	3.5
14. K610 - Anal abscess	781	0	0.0	1.2	5.6
15. J690 - Pneumonitis due to food and vomit	776	260	33.5	14.1	5.0
16. K579 - Diverticular disease of intestine, part unspecified, without perforation or abscess	718	1	0.1	1.3	2.1
17. L024 - Cutaneous abscess, furuncle and carbuncle of limb	710	0	0.0	2.5	5.6
18. L050 - Pilonidal cyst with abscess	533	0	0.0	0.6	4.9
19. L022 - Cutaneous abscess, furuncle and carbuncle of trunk	527	1	0.2	2.5	8.2
20. O234 - Unspecified infection of urinary tract in pregnancy	518	0	0.0	1.3	1.0
21. K800 - Calculus of gallbladder with acute cholecystitis	517	6	1.2	4.7	8.5
22. K37X - Unspecified appendicitis	505	1	0.2	2.5	3.8
23. J180 - Bronchopneumonia, unspecified	432	242	56.0	10.5	5.8
24. J36X - Peritonsillar abscess	429	0	0.0	1.3	2.8
25. N459 - Orchitis, epididymitis and epididymo-orchitis without abscess	413	0	0.0	1.8	6.1
	***n* = 44370**	***n* = 2977**	***m* = 6.3**	***m* = 4.7**	***n* = 5.9**

Table 2: **Top ten "Suspicion of Sepsis" diagnoses associated with death in Oxford AHSN region (2013-14)**

Diagnosis	No. of Deaths	No. of admissions	Mortality (%)	LOS	Readmission (%)
1. J181 - Lobar pneumonia, unspecified	990	5265	18.8	9.8	6.3
2. J189 - Pneumonia, unspecified	483	3126	15.5	9.6	7.1
3. N390 - Urinary tract infection, site not specified	285	7088	4.0	9.0	6.4
4. A419 - Sepsis, unspecified	280	1882	14.9	9.2	10.7
5. J690 - Pneumonitis due to food and vomit	260	776	33.5	14.1	5.0
6. J180 - Bronchopneumonia, unspecified	242	432	56.0	10.5	5.8
7. J440 - Chronic obstructive pulmonary disease with acute lower respiratory infection	184	2854	6.4	7.2	11.3
8. J22X - Unspecified acute lower respiratory infection	167	3808	4.4	6.5	7.4
9. L031 - Cellulitis of other parts of limb	62	2983	2.1	6.9	7.5
10. K631 - Perforation of intestine (nontraumatic)	51	136	37.5	13.0	5.9
	***n* = 3004**	***n* = 28350**	***m* = 19.3**	***m* = 9.6**	***m* = 7.3**

Figure 1: **Suspicion of sepsis admissions and mortality by age and gender**

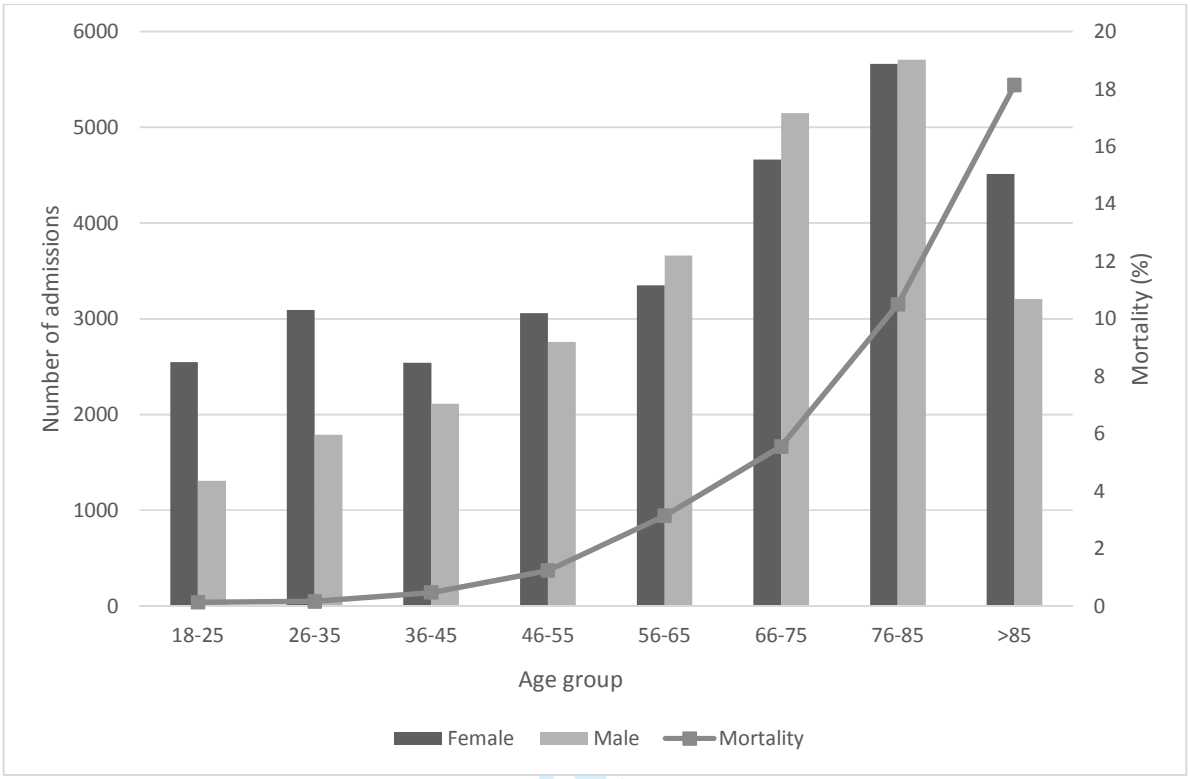
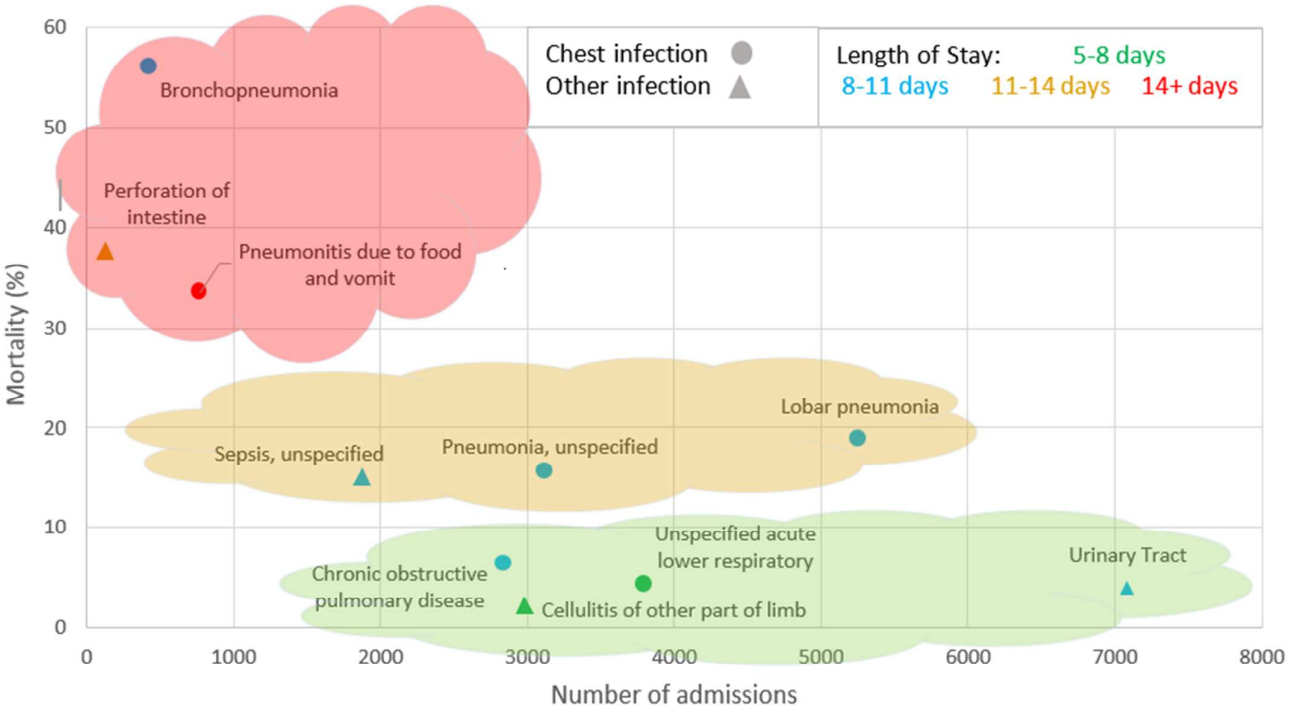


Figure 2: **Top 10 "Suspicion of sepsis" diagnoses associated with death**



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Contributors: MIK conceived the study. IM carried out the analysis and BP prepared all tables and figures. BP and CV prepared the first draft of the paper. All authors provided critical feedback and contributions to the final paper.

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Competing interests: MIK reports grants for roles as clinical lead for sepsis across Oxford Academic Health Science Network and clinical lead of the Patient Safety Collaborative, Wessex. BP and IM declare no competing interests. CV declares grants from Oxford Academic Health Science Network, during the conduct of the study and occasional consultancy work on patient safety unrelated to this project.

Ethical approval: Not required as the data was routinely collected hospital administrative data and not in a patient identifiable format.

Data sharing: A full list of the suspicion of sepsis ICD-10 codes is given in Appendix A. Additional information on methodology can be obtained from the corresponding author on request. No additional data is available.

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APPENDIX A

"Suspicion of sepsis" coding set: ICD-10 bacterial infection codes

I. Certain Infectious and parasitic diseases

1. A01 Typhoid and paratyphoid fevers (incl. A01.0, A01.1, A01.2, A01.3, A01.4)
2. A02 Other salmonella infections (incl. A02.0, A02.1, A02.2, A02.8, A02.9)
3. A03 Shigellosis (incl. A03.0, A03.1, A03.2, A03.3, A03.8, A03.9)
4. A04 Other bacterial intestinal infections (incl. A04.0, A04.1, A04.2, A04.3, A04.4, A04.5, A04.6, A04.7, A04.8, A04.9)
5. A06 Amoebiasis (incl. A06.0, A06.1, A06.2, A06.3, A06.4, A06.5, A06.6, A06.7, A06.7, A06.8, A06.9)
6. A15 Respiratory tuberculosis (incl. A15.0, A15.2, A15.3, A15.4, A15.5, A15.6, A15.7, A15.8, A15.9)
7. A16 Respiratory tuberculosis, not confirmed bacteriologically or histologically (incl. A16.0, A16.1, A16.2, A16.3, A16.4, A16.5, A16.7, A16.8, A16.9)
8. A17 Tuberculosis of nervous system (incl. A17.0, A17.1, A17.8, A17.9)
9. A18 Tuberculosis of other organs (incl. A18.0, A18.1, A18.2, A18.3, A18.4, A18.5, A18.6, A18.7, A18.8)
10. A19 Miliary tuberculosis (incl. A19.0, A19.1, A19.2, A19.8, A19.9)
11. A27 Leptospirosis (incl. A27.0, A27.8, A27.9)
12. A32 Listerosis (incl. A32.0, A32.1, A32.7, A32.8, A32.9)
13. A37 Whopping cough (all subcategories)
14. A38 Scarlet fever
15. A39 Meningococcal infection (incl. A39.0, A39.1, A39.2, A39.4, A39.5, A39.8, A39.9)
16. A40 Streptococcal sepsis (incl. A40.0, A40.1, A40.2, A40.3, A40.8, A40.9)
17. A41 Other Sepsis (incl. A41.0, A41.1, A41.2, A41.3, A41.4, A41.5, A41.8, A41.9)
18. A42 Actinomycosis (all subcategories)
19. A43 Nocardiosis (all subcategories)
20. A44 Bartenollosis (all subcategories)
21. A46 Erysipelas
22. A48 Other Bacterial diseases, not elsewhere classified (incl. A48.0, A48.1, A48.2, A48.3, A48.4, A48.8)
23. A49 Bacterial infection of unspecified site (incl. A49.0, A49.1, A49.2, A49.3, A49.8, A49.8, A49.9)
24. A51 Early syphilis (all subcategories)
25. A54 Gonococcal infection (incl. A54.1, A54.2, A54.3, A54.4, A54.5, A54.6, A54.8, A54.9)
26. A55 Chlamydial lymhogranuloma (venereum)
27. A56 Other sexually transmitted chlamydial diseases (incl. A56.0, A56.1, A56.2, A56.3, A56.4, A56.8)
28. A68 Relapsing fevers (all subcategories)
29. A69.2 Lyme disease
30. A70 Chlamydia psittaci infection

31. A75 Typhus fever (all subcategories)
32. A77 Spotted fever (all subcategories)
33. A78 Q fever
34. A79 Other rickettsioses (all subcategories)
35. B59 Pneumocystosis

VI. Diseases of the nervous system

36. G00 Bacterial meningitis, not elsewhere classified (incl. G00.0, G00.1, G00.2, G00.3, G00.8, G00.9)
37. G01 Meningitis in bacterial diseases classified elsewhere
38. G04.2 Bacterial meningoencephalitis and meningomyelitis, not elsewhere classified
39. G06 Intracranial and intraspinal abscess and granuloma (incl. G06.0, G06.1, G06.2)

VIII. Diseases of the ear and mastoid process

40. H60 Otitis externa (incl. H60.0, H60.1, H60.2, H60.3)
41. H66 Suppurative and unspecified otitis media (incl. H66.0, H66.4, H66.9)
42. H67.0 Otitis media in bacterial diseases classified elsewhere
43. H68.0 eustachian salpingitis
44. H70 Mastoiditis and related conditions (incl. H70.0, H70.9)
45. H73.0 Acute myringitis

IX. Diseases of the circulatory system

46. I00 Rheumatic fever without mention of heart involvement
47. I01 Rheumatic fever with heart involvement (incl. I01.0, I01.1, I01.2, I01.8, I01.9)
48. I02 Rheumatic chorea (incl. I02.0, I02.9)
49. I33 Acute and subacute endocarditis (incl. I33.0, I33.9)
50. I38 Endocarditis, valve unspecified
51. I39 Endocarditis and heart valve disorders in diseases classified elsewhere (incl. I39.0, I39.1, I39.2, I39.3, I39.4, I39.8)
52. I41.0 Myocarditis in bacterial diseases classified elsewhere

X. Diseases of the respiratory system

53. J01 Acute sinusitis (incl. J01.0, J01.1, J01.2, J01.3, J01.4, J01.8, J01.9)
54. J02 Acute pharyngitis (incl. J02.0, J02.9)
55. J03 Acute tonsillitis (incl. J03.0, J03.9)
56. J05.1 Acute epiglottitis
57. J06.9 Acute upper respiratory infection, unspecified
58. J13 Pneumonia due to Streptococcus pneumoniae,
59. J14 Pneumonia due to Haemophilus influenza,
60. J15 Bacterial pneumonia, not elsewhere classified (J15.0, J15.1, J15.2, J15.3, J15.4, J15.5, J15.6, J15.7, J15.8, J15.9)

61. J16 Pneumonia due to other infectious organisms, not elsewhere classified (incl. J16.0, J16.8)]
62. J17.0 Pneumonia in bacterial diseases classified elsewhere (incl. J17.0, J17.8)
63. J18 Pneumonia, organism unspecified (including J18.0, J18.1, J18.2, J18.8 and J18.9)
64. J20 Acute bronchitis (incl. J20.0, J20.1, J20.2, J20.8, J20.9)
65. J22 Unspecified acute lower respiratory infection
66. J36 Peritonsillar abscess
67. J39 Other diseases of upper respiratory tract (incl. J39.0, J39.1)
68. J44.0 Chronic obstructive pulmonary disease with acute lower respiratory infection
69. J69 Pneumonitis due to solids and liquids (incl. J69.0, J69.8)
70. J84.9 Interstitial pulmonary disease unspecified (interstitial pneumonia NOS)
71. J85 Abscess of lung and mediastinum (incl. J85.1, J85.2, J85.3)
72. J86 Pyothorax (incl. J86.0, J86.9)
73. J95.0 Sepsis of tracheostomy stoma
74. J98.5 Diseases of mediastinum, not elsewhere classified- Mediastinitis

XI. Diseases of the digestives system (dental disorders omitted)

75. K22.3 Perforation of oesophagus
76. K35 Acute appendicitis (incl. K35.2, K35.3, K35.8)
77. K37 Unspecified appendicitis
78. K57 Diverticular disease of intestine (incl. K57.0, K57.1, K57.2, K57.3, K57.4, K57.5,K57.8, K57.9)
79. K61 Abscess of anal and rectal regions (incl. K61.0, K61.1, K61.2, K61.3, 61.4)
80. K63.0 Abscess of intestine
81. K63.1 Perforation of intestine (nontraumatic)
82. K65.0 Acute peritonitis (incl. K65.0, K65.8, K65.9)
83. K67 Disorders of peritoneum in infectious diseases classified elsewhere (all subcategories)
84. K75.0 Abscess of liver
85. K80.0 Calculus of gallbladder with acute cholecystitis/cholangitis (incl.K80.0, K80.1, K80.3, K80.4, K80.5)
86. K81 Cholecystitis (incl. K81.0, K81.1, K81.8, K81.9)
87. K82.2 Perforation of gallbladder
88. K83.0 Cholangitis
89. K83.2 Perforation of bile duct

XII. Diseases of skin and subcutaneous tissue

90. L00 Staphylococcal scalded skin syndrome
91. L01 Impetigo (L01.0, L01.1)
92. L02 Cutaneous abscess, furuncle and carbuncle (incl. L02.0, L02.1, L02.2, L02.3, L02.4, L02.8, L02.9)
93. L03 Cellulitis (including L03.0, L03.1, L03.2, L03.3, L03.8 and L03.9)
94. L05.0 Pilonidal cyst with abscess
95. L08 Other local infections of skin and subcutaneous tissue (incl. L08.0, L08.8, L08.9)

96. L30.3 Infective dermatitis
97. L53.3 Erythema marginatum
98. L98.0 Pyogenic granuloma

XIII. Diseases of the musculoskeletal system and connective tissue

99. M00 Pyogenic arthritis (incl. M00.0, M00.1, M00.2, M00.8, M00.9)
100. M01 Direct infections of joint in infectious and parasitic diseases classified elsewhere (incl. M01.0, M01.1, M01.2, M01.3)
101. M46.2 Osteomyelitis of vertebra
102. M46.4 Discitis, unspecified
103. M65 Synovitis and tenosynovitis (incl. M65.0, M65.1)
104. M71.0 Abscess of bursa
105. M72.6 Necrotizing fasciitis
106. M86 Osteomyelitis

XIV. Diseases of genitourinary system

107. N10 Acute tubulo-interstitial nephritis
108. N11 Chronic tubulo-interstitial nephritis (incl. N11.0, N11.1, N11.8, N11.9)
109. N12 Tubulo-intestitial nephritis, not specified as acute or chronic
110. N13.6 Pyonephrosis
111. N15.1 Renal and perinephric abscess
112. N15.9 Renal tubulo-interstitial disease, unspecified
113. N30 Cystitis, unspecified (including N30.0, N30.8, N30.9)
114. N34.0 Urethral abscess
115. N39.0 Urinary tract infection, site not specified
116. N41.0 Acute prostatitis
117. N43.1 Infected hydrocele
118. N45 Orchitis and epididymitis (incl. N45.0, N45.9)
119. N48.2 Other disorders of penis (incl. N48.1, N48.2)
120. N49.9 Inflammatory disorder of unspecified male genital organ
121. N61 Inflammatory disorders of breast
122. N70 Salpingitis and oophoritis (incl N70.0, N70.9)
123. N71 Inflammatory disease of uterus, except cervix (incl. N71.0, N71.9)
124. N73 Other female pelvic inflammatory diseases (incl. N73.0, N73.1, N73.2, N73.4, N73.9)
125. N75.1 Abscess of Bartholin gland
126. N76 Other inflammation of vagina and vulva (incl. N76.0, N76.1, N76.3, N76.4, N76.8)

XV. Pregnancy, Childbirth and the puerperium

127. O08.0 Genital tract and pelvic infection following abortion and ectopic and molar pregnancy

128. O23 Infections of genitourinary tract in pregnancy (incl. O23.0, O23.1, O23.2, O23.3, O23.4, O23.5, O23.9)
129. O41.1 Infection of amniotic sac and membranes
130. 085 Puerperal sepsis
131. 086 Other puerperal infections (incl. O86.0, O86.1, O86.2, O86.3, O86.4, O86.8)
132. O88.3 Obstetric pyaemic and septic embolism
133. 091 Infections of breast associated with childbirth (incl. O91.0, O91.1)

XVI. Certain conditions originating in the perinatal period

134. P36 Bacterial sepsis of newborn (incl. P36.0, P36.1, P36.2, P36.3, P36.4, P36.5, P36.8, P36.9)
135. P39 Other infections specific to the perinatal period (incl. P39.0, P39.2, P39.3, P39.4, P39.8, P39.9)
136. P78 Other perinatal digestives system disorders (P78.0, P78.1,)
137. T814 Infection following a procedure, not elsewhere classified,
138. T845 Infection and inflammatory reaction due to internal joint prosthesis

XVIII. Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified

139. R57.2 Septic shock
140. R65 Systemic Inflammatory Response syndrome (incl. R65.0, R65.1, R65.9)

Note: Codes B95-98 were not considered since they should never be used in primary coding. http://apps.who.int/classifications/icd10/browse/2016/en#/B95-B98

APPENDIX B

Full table of "suspicion of sepsis" diagnoses: number of admissions, deaths, mortality, length of stay and readmission rate

Diagnosis	No. of admissions	No. of deaths	Mortality (%)	LOS	Readmissions (%)
1. N390 - Urinary tract infection, site not specified	7088	285	4.0	9.0	6.4
2. K573 - Diverticular disease of large intestine without perforation or abscess	5414	9	0.2	0.8	1.3
3. J181 - Lobar pneumonia, unspecified	5265	990	18.8	9.8	6.3
4. J22X - Unspecified acute lower respiratory infection	3808	167	4.4	6.5	7.4
5. J189 - Pneumonia, unspecified	3126	483	15.5	9.6	7.1
6. L031 - Cellulitis of other parts of limb	2983	62	2.1	6.9	7.5
7. J440 - Chronic obstructive pulmonary disease with acute lower respiratory infection	2854	184	6.4	7.2	11.3
8. A419 - Sepsis, unspecified	1882	280	14.9	9.2	10.7
9. K805 - Calculus of bile duct without cholangitis or cholecystitis	1167	2	0.2	1.7	7.6
10. T814 - Infection following a procedure, not elsewhere classified	1067	3	0.3	5.9	7.7
11. J039 - Acute tonsillitis, unspecified	1055	0	0.0	1.2	5.7
12. K358 - Acute appendicitis, other and unspecified	993	0	0.0	2.9	6.4
13. N12X - Tubulo-interstitial nephritis, not specified as acute or chronic	809	1	0.1	3.5	3.5
14. K610 - Anal abscess	781	0	0.0	1.2	5.6
15. J690 - Pneumonitis due to food and vomit	776	260	33.5	14.1	5.0
16. K579 - Diverticular disease of intestine, part unspecified, without perforation or abscess	718	1	0.1	1.3	2.1
17. L024 - Cutaneous abscess, furuncle and carbuncle of limb	710	0	0.0	2.5	5.6
18. L050 - Pilonidal cyst with abscess	533	0	0.0	0.6	4.9
19. L022 - Cutaneous abscess, furuncle and carbuncle of trunk	527	1	0.2	2.5	8.2
20. O234 - Unspecified infection of urinary tract in pregnancy	518	0	0.0	1.3	1.0
21. K800 - Calculus of gallbladder with acute cholecystitis	517	6	1.2	4.7	8.5
22. K37X - Unspecified appendicitis	505	1	0.2	2.5	3.8

23. J180 - Bronchopneumonia, unspecified	432	242	56.0	10.5	5.8
24. J36X - Peritonsillar abscess	429	0	0.0	1.3	2.8
25. N459 - Orchitis, epididymitis and epididymo-orchitis without abscess	413	0	0.0	1.8	6.1
26. A415 - Sepsis due to other Gram-negative organisms	360	40	11.1	11.5	10.8
27. T845 - Infection and inflammatory reaction due to internal joint prosthesis	345	4	1.2	19.1	5.5
28. K819 - Cholecystitis, unspecified	339	5	1.5	4.0	8.8
29. K353 - Acute appendicitis with localized peritonitis	318	2	0.6	5.2	6.6
30. K810 - Acute cholecystitis	312	7	2.2	6.0	8.3
31. M869 - Osteomyelitis, unspecified	310	7	2.3	14.8	9.4
32. N309 - Cystitis, unspecified	291	0	0.0	0.6	1.0
33. L030 - Cellulitis of finger and toe	289	1	0.3	3.0	4.2
34. K830 - Cholangitis	240	18	7.5	9.5	4.6
35. K811 - Chronic cholecystitis	237	0	0.0	1.7	5.9
36. K572 - Diverticular disease of large intestine with perforation and abscess	231	20	8.7	12.5	8.7
37. N61X - Inflammatory disorders of breast	231	0	0.0	1.1	7.8
38. A047 - Enterocolitis due to Clostridium difficile	208	20	9.6	16.1	11.1
39. O860 - Infection of obstetric surgical wound	202	0	0.0	2.0	0.0
40. J069 - Acute upper respiratory infection, unspecified	190	1	0.5	1.1	7.9
41. L023 - Cutaneous abscess, furuncle and carbuncle of buttock	189	0	0.0	1.3	8.5
42. N739 - Female pelvic inflammatory disease, unspecified	180	0	0.0	2.9	7.8
43. J029 - Acute pharyngitis, unspecified	169	0	0.0	0.9	7.7
44. L089 - Local infection of skin and subcutaneous tissue, unspecified	165	1	0.6	3.8	4.8
45. N751 - Abscess of Bartholin's gland	159	0	0.0	0.8	2.5
46. M009 - Pyogenic arthritis, unspecified	140	5	3.6	11.9	6.4
47. A045 - Campylobacter enteritis	136	3	2.2	6.6	2.2
48. K803 - Calculus of bile duct with cholangitis	136	7	5.1	10.6	2.9
49. K631 - Perforation of intestine (nontraumatic)	136	51	37.5	13.0	5.9
50. L033 - Cellulitis of trunk	127	0	0.0	5.2	7.1
51. L032 - Cellulitis of face	124	0	0.0	3.2	1.6

52. K804 - Calculus of bile duct with cholecystitis	117	2	1.7	6.8	9.4
53. J869 - Pyothorax without fistula	114	7	6.1	13.0	8.8
54. H669 - Otitis media, unspecified	113	0	0.0	1.6	0.9
55. J13X - Pneumonia due to Streptococcus pneumoniae	112	11	9.8	11.0	2.7
56. N308 - Other cystitis	109	0	0.0	0.9	0.9
57. N10X - Acute tubulo-interstitial nephritis	108	1	0.9	4.0	4.6
58. O85X - Puerperal sepsis	107	0	0.0	2.8	1.9
59. M866 - Other chronic osteomyelitis	103	0	0.0	12.7	4.9
60. K650 - Acute peritonitis	96	13	13.5	12.6	14.6
61. N136 - Pyonephrosis	93	6	6.5	14.8	5.4
62. I330 - Acute and subacute infective endocarditis	89	11	12.4	21.3	9.0
63. A418 - Other specified sepsis	87	32	36.8	10.5	9.2
64. A048 - Other specified bacterial intestinal infections	82	1	1.2	1.2	2.4
65. J849 - Interstitial pulmonary disease, unspecified	80	9	11.3	5.2	3.8
66. L980 - Pyogenic granuloma	80	0	0.0	0.1	3.8
67. K613 - Ischiorectal abscess	80	0	0.0	3.4	10.0
68. N764 - Abscess of vulva	73	0	0.0	1.4	4.1
69. A410 - Sepsis due to Staphylococcus aureus	70	24	34.3	17.7	1.4
70. O230 - Infections of kidney in pregnancy	66	0	0.0	2.9	0.0
71. M464 - Discitis, unspecified	65	1	1.5	17.9	4.6
72. M864 - Chronic osteomyelitis with draining sinus	65	0	0.0	15.4	1.5
73. O864 - Pyrexia of unknown origin following delivery	61	0	0.0	2.5	0.0
74. L021 - Cutaneous abscess, furuncle and carbuncle of neck	60	0	0.0	3.1	1.7
75. O235 - Infections of the genital tract in pregnancy	59	0	0.0	0.7	0.0
76. N719 - Inflammatory disease of uterus, unspecified	57	1	1.8	2.5	1.8
77. J209 - Acute bronchitis, unspecified	52	0	0.0	2.7	1.9
78. K659 - Peritonitis, unspecified	52	18	34.6	6.2	1.9
79. J151 - Pneumonia due to Pseudomonas	51	14	27.5	17.9	7.8
80. N709 - Salpingitis and oophoritis, unspecified	48	0	0.0	5.3	0.0
81. K750 - Abscess of liver	46	2	4.3	13.6	6.5
82. N410 - Acute prostatitis	45	0	0.0	0.8	0.0
83. M651 - Other infective (teno)synovitis	44	0	0.0	7.0	4.5

84. A498 - Other bacterial infections of unspecified site	44	4	9.1	11.6	13.6
85. L039 - Cellulitis, unspecified	44	3	6.8	6.1	11.4
86. O411 - Infection of amniotic sac and membranes	42	0	0.0	6.2	0.0
87. M000 - Staphylococcal arthritis and polyarthritis	41	1	2.4	14.8	2.4
88. A411 - Sepsis due to other specified staphylococcus	40	9	22.5	11.1	12.5
89. K571 - Diverticular disease of small intestine without perforation or abscess	39	0	0.0	1.4	2.6
90. N119 - Chronic tubulo-interstitial nephritis, unspecified	38	0	0.0	3.9	2.6
91. O862 - Urinary tract infection following delivery	38	0	0.0	1.6	0.0
92. M726 - Necrotizing fasciitis	38	11	28.9	20.4	2.6
93. N481 - Balanoposthitis	38	0	0.0	0.3	2.6
94. J019 - Acute sinusitis, unspecified	37	0	0.0	1.0	2.7
95. M868 - Other osteomyelitis	35	0	0.0	1.5	2.9
96. H601 - Cellulitis of external ear	35	0	0.0	2.4	0.0
97. A490 - Staphylococcal infection, unspecified site	34	5	14.7	14.5	8.8
98. A408 - Other streptococcal sepsis	34	6	17.6	16.1	5.9
99. L020 - Cutaneous abscess, furuncle and carbuncle of face	34	0	0.0	1.9	0.0
100. J051 - Acute epiglottitis	32	1	3.1	3.4	3.1
101. J14X - Pneumonia due to Haemophilus influenzae	32	3	9.4	9.1	3.1
102. N482 - Other inflammatory disorders of penis	30	0	0.0	2.4	3.3
103. N450 - Orchitis, epididymitis and epididymo-orchitis with abscess	29	0	0.0	4.4	0.0
104. O911 - Abscess of breast associated with childbirth	29	0	0.0	2.0	17.2
105. M861 - Other acute osteomyelitis	28	0	0.0	16.1	7.1
106. J150 - Pneumonia due to Klebsiella pneumoniae	27	8	29.6	15.6	7.4
107. H602 - Malignant otitis externa	27	0	0.0	20.3	3.7
108. J390 - Retropharyngeal and parapharyngeal abscess	26	0	0.0	6.0	3.8
109. J860 - Pyothorax with fistula	26	0	0.0	13.9	3.8
110. A46X - Erysipelas	25	0	0.0	1.7	0.0
111. L038 - Cellulitis of other sites	25	0	0.0	3.7	4.0
112. L303 - Infective dermatitis	23	0	0.0	3.5	13.0
113. J950 - Tracheostomy malfunction	23	1	4.3	5.1	21.7
114. G060 - Intracranial abscess and	22	1	4.5	22.6	0.0

granuloma					
115. N300 - Acute cystitis	22	0	0.0	3.0	4.5
116. R572 - Septic shock	21	11	52.4	11.2	9.5
117. A409 - Streptococcal sepsis, unspecified	21	3	14.3	14.9	9.5
118. A169 - Respiratory tuberculosis unspecified, without mention of bacteriological or histological confirmation	20	1	5.0	6.8	5.0
119. G009 - Bacterial meningitis, unspecified	20	2	10.0	12.1	0.0
120. A499 - Bacterial infection, unspecified	19	3	15.8	8.7	10.5
121. A400 - Sepsis due to streptococcus, group A	19	4	21.1	11.6	0.0
122. J154 - Pneumonia due to other streptococci	19	4	21.1	11.1	0.0
123. O231 - Infections of bladder in pregnancy	19	0	0.0	1.7	5.3
124. A412 - Sepsis due to unspecified staphylococcus	19	4	21.1	16.8	21.1
125. N151 - Renal and perinephric abscess	19	1	5.3	11.3	5.3
126. J208 - Acute bronchitis due to other specified organisms	19	0	0.0	3.0	0.0
127. H600 - Abscess of external ear	18	0	0.0	1.3	11.1
128. J152 - Pneumonia due to staphylococcus	18	5	27.8	19.7	11.1
129. A180 - Tuberculosis of bones and joints	18	0	0.0	9.4	11.1
130. M002 - Other streptococcal arthritis and polyarthritis	18	0	0.0	14.2	11.1
131. H709 - Mastoiditis, unspecified	18	0	0.0	3.1	5.6
132. A491 - Streptococcal infection, unspecified site	17	1	5.9	11.5	5.9
133. J698 - Pneumonitis due to other solids and liquids	17	5	29.4	12.2	5.9
134. A403 - Sepsis due to Streptococcus pneumoniae	16	2	12.5	10.7	0.0
135. O861 - Other infection of genital tract following delivery	16	0	0.0	2.2	0.0
136. A162 - Tuberculosis of lung, without mention of bacteriological or histological confirmation	16	2	12.5	8.9	0.0
137. A020 - Salmonella enteritis	15	0	0.0	7.0	6.7
138. G061 - Intraspinal abscess and granuloma	15	0	0.0	48.1	13.3
139. K658 - Other peritonitis	15	3	20.0	8.1	6.7
140. L088 - Other specified local infections of skin and subcutaneous tissue	15	0	0.0	6.4	0.0

141. A481 - Legionnaires' disease	14	0	0.0	12.5	0.0
142. B59X - Pneumocystosis	14	5	35.7	15.6	21.4
143. N111 - Chronic obstructive pyelonephritis	14	0	0.0	4.2	0.0
144. K223 - Perforation of oesophagus	14	2	14.3	16.4	7.1
145. G001 - Pneumococcal meningitis	14	0	0.0	12.9	7.1
146. M008 - Arthritis and polyarthritis due to other specified bacterial agents	14	0	0.0	25.6	0.0
147. J985 - Diseases of mediastinum, not elsewhere classified	14	1	7.1	7.1	7.1
148. K611 - Rectal abscess	13	1	7.7	9.1	0.0
149. M650 - Abscess of tendon sheath	13	0	0.0	4.2	0.0
150. A401 - Sepsis due to streptococcus, group B	12	1	8.3	20.2	0.0
151. O080 - Genital tract and pelvic infection following abortion and ectopic and molar pregnancy	12	0	0.0	1.9	16.7
152. K630 - Abscess of intestine	12	0	0.0	9.3	16.7
153. O233 - Infections of other parts of urinary tract in pregnancy	11	0	0.0	1.9	18.2
154. A010 - Typhoid fever	11	0	0.0	7.9	9.1
155. H603 - Other infective otitis externa	10	0	0.0	2.2	30.0
156. A150 - Tuberculosis of lung, confirmed by sputum microscopy with or without culture	10	1	10.0	5.8	0.0
157. J851 - Abscess of lung with pneumonia	10	0	0.0	16.4	10.0
158. J188 - Other pneumonia, organism unspecified	10	0	0.0	2.5	0.0
159. J158 - Other bacterial pneumonia	9	1	11.1	15.2	0.0
160. A049 - Bacterial intestinal infection, unspecified	9	0	0.0	10.4	11.1
161. K574 - Diverticular disease of both small and large intestine with perforation and abscess	9	1	11.1	20.3	0.0
162. K822 - Perforation of gallbladder	9	0	0.0	22.7	11.1
163. N768 - Other specified inflammation of vagina and vulva	9	0	0.0	0.3	0.0
164. M462 - Osteomyelitis of vertebra	9	0	0.0	29.7	0.0
165. J852 - Abscess of lung without pneumonia	9	1	11.1	8.3	22.2
166. J391 - Other abscess of pharynx	8	0	0.0	4.6	0.0
167. A182 - Tuberculous peripheral lymphadenopathy	8	0	0.0	0.1	12.5
168. N760 - Acute vaginitis	8	0	0.0	2.4	0.0
169. L028 - Cutaneous abscess, furuncle and carbuncle of other sites	8	0	0.0	3.1	0.0

170. A414 - Sepsis due to anaerobes	8	0	0.0	12.9	12.5
171. L029 - Cutaneous abscess, furuncle and carbuncle, unspecified	8	0	0.0	0.5	0.0
172. A165 - Tuberculous pleurisy, without mention of bacteriological or histological confirmation	8	0	0.0	6.6	0.0
173. A402 - Sepsis due to streptococcus, group D	8	0	0.0	12.1	0.0
174. K570 - Diverticular disease of small intestine with perforation and abscess	8	2	25.0	11.1	0.0
175. J155 - Pneumonia due to Escherichia coli	8	2	25.0	10.4	0.0
176. K612 - Anorectal abscess	8	0	0.0	0.5	0.0
177. N110 - Nonobstructive reflux-associated chronic pyelonephritis	8	0	0.0	3.1	0.0
178. O868 - Other specified puerperal infections	8	0	0.0	1.9	0.0
179. K614 - Intrasphincteric abscess	7	0	0.0	2.0	0.0
180. M011 - Tuberculous arthritis	7	0	0.0	9.6	28.6
181. A692 - Lyme disease	7	0	0.0	29.6	14.3
182. G002 - Streptococcal meningitis	6	1	16.7	12.5	0.0
183. A390 - Meningococcal meningitis	6	0	0.0	9.3	0.0
184. I339 - Acute endocarditis, unspecified	6	0	0.0	22.3	0.0
185. A394 - Meningococcaemia, unspecified	6	0	0.0	8.2	16.7
186. J156 - Pneumonia due to other aerobic Gram-negative bacteria	6	0	0.0	13.0	0.0
187. J010 - Acute maxillary sinusitis	6	0	0.0	2.5	0.0
188. O239 - Other and unspecified genitourinary tract infection in pregnancy	6	0	0.0	0.5	0.0
189. H660 - Acute suppurative otitis media	6	0	0.0	3.5	0.0
190. J159 - Bacterial pneumonia, unspecified	6	0	0.0	3.0	16.7
191. K818 - Other cholecystitis	6	0	0.0	2.7	0.0
192. A044 - Other intestinal Escherichia coli infections	6	0	0.0	8.8	0.0
193. M710 - Abscess of bursa	6	0	0.0	1.8	0.0
194. M863 - Chronic multifocal osteomyelitis	6	0	0.0	0.0	0.0
195. A152 - Tuberculosis of lung, confirmed histologically	6	0	0.0	11.7	16.7
196. N340 - Urethral abscess	6	0	0.0	1.3	0.0
197. L010 - Impetigo [any organism] [any site]	5	0	0.0	2.2	20.0
198. A199 - Miliary tuberculosis, unspecified	5	2	40.0	29.0	20.0

199. H664 - Suppurative otitis media, unspecified	5	0	0.0	1.0	0.0
200. A379 - Whooping cough, unspecified	5	0	0.0	1.8	0.0
201. A183 - Tuberculosis of intestines, peritoneum and mesenteric glands	5	0	0.0	25.6	20.0
202. A156 - Tuberculous pleurisy, confirmed bacteriologically and histologically	5	1	20.0	18.4	0.0
203. A428 - Other forms of actinomycosis	5	0	0.0	6.8	0.0
204. N710 - Acute inflammatory disease of uterus	5	0	0.0	0.6	0.0
205. A039 - Shigellosis, unspecified	4	0	0.0	5.8	0.0
206. A170 - Tuberculous meningitis	4	0	0.0	41.5	0.0
207. G062 - Extradural and subdural abscess, unspecified	4	1	25.0	39.0	0.0
208. A178 - Other tuberculosis of nervous system	4	1	25.0	16.3	0.0
209. H700 - Acute mastoiditis	4	0	0.0	2.0	0.0
210. J020 - Streptococcal pharyngitis	4	0	0.0	2.3	25.0
211. A561 - Chlamydial infection of pelviperitoneum and other genitourinary organs	4	0	0.0	2.5	0.0
212. A398 - Other meningococcal infections	4	0	0.0	31.0	0.0
213. J030 - Streptococcal tonsillitis	3	0	0.0	1.7	0.0
214. A184 - Tuberculosis of skin and subcutaneous tissue	3	0	0.0	4.3	0.0
215. J018 - Other acute sinusitis	3	0	0.0	1.0	0.0
216. G042 - Bacterial meningoencephalitis and meningomyelitis, not elsewhere classified	3	1	33.3	14.3	0.0
217. A191 - Acute miliary tuberculosis of multiple sites	3	0	0.0	12.0	0.0
218. N431 - Infected hydrocele	3	0	0.0	2.7	0.0
219. N159 - Renal tubulo-interstitial disease, unspecified	3	0	0.0	2.3	0.0
220. N730 - Acute parametritis and pelvic cellulitis	3	0	0.0	4.7	0.0
221. A181 - Tuberculosis of genitourinary system	3	0	0.0	0.7	33.3
222. N700 - Acute salpingitis and oophoritis	3	0	0.0	5.0	0.0
223. A011 - Paratyphoid fever A	3	0	0.0	6.7	0.0
224. N118 - Other chronic tubulo-interstitial nephritis	2	0	0.0	9.0	0.0
225. A190 - Acute miliary tuberculosis of a single specified site	2	0	0.0	33.5	50.0

226. A270 - Leptospirosis icterohaemorrhagica	2	0	0.0	0.0	50.0
227. A153 - Tuberculosis of lung, confirmed by unspecified means	2	0	0.0	10.0	0.0
228. M860 - Acute haematogenous osteomyelitis	2	0	0.0	10.0	0.0
229. A483 - Toxic shock syndrome	2	0	0.0	10.5	0.0
230. A279 - Leptospirosis, unspecified	2	0	0.0	4.5	0.0
231. J157 - Pneumonia due to Mycoplasma pneumoniae	2	0	0.0	9.0	0.0
232. A029 - Salmonella infection, unspecified	2	0	0.0	5.0	0.0
233. N731 - Chronic parametritis and pelvic cellulitis	2	0	0.0	3.0	0.0
234. L011 - Impetiginization of other dermatoses	2	0	0.0	2.0	0.0
235. A327 - Listerial sepsis	2	0	0.0	17.0	50.0
236. A021 - Salmonella sepsis	2	0	0.0	10.5	50.0
237. J012 - Acute ethmoidal sinusitis	2	0	0.0	6.0	0.0
238. A321 - Listerial meningitis and meningoencephalitis	2	0	0.0	25.0	0.0
239. J011 - Acute frontal sinusitis	2	0	0.0	1.0	0.0
240. O863 - Other genitourinary tract infections following delivery	2	0	0.0	1.5	0.0
241. A329 - Listeriosis, unspecified	2	0	0.0	20.5	0.0
242. N763 - Subacute and chronic vulvitis	2	0	0.0	0.0	0.0
243. A033 - Shigellosis due to Shigella sonnei	2	0	0.0	4.0	0.0
244. A413 - Sepsis due to Haemophilus influenzae	1	0	0.0	18.0	0.0
245. A420 - Pulmonary actinomycosis	1	0	0.0	21.0	0.0
246. H730 - Acute myringitis	1	0	0.0	0.0	0.0
247. J153 - Pneumonia due to streptococcus, group B	1	0	0.0	84.0	0.0
248. A157 - Primary respiratory tuberculosis, confirmed bacteriologically and histologically	1	0	0.0	0.0	100.0
249. A171 - Meningeal tuberculoma	1	0	0.0	5.0	0.0
250. L080 - Pyoderma	1	0	0.0	3.0	0.0
251. A159 - Respiratory tuberculosis unspecified, confirmed bacteriologically and histologically	1	0	0.0	9.0	0.0
252. N499 - Inflammatory disorder of unspecified male genital organ	1	0	0.0	1.0	0.0
253. J182 - Hypostatic pneumonia, unspecified	1	0	0.0	7.0	0.0
254. M865 - Other chronic haematogenous osteomyelitis	1	0	0.0	13.0	0.0
255. A422 - Cervicofacial	1	0	0.0	0.0	0.0

actinomycosis					
256. A164 - Tuberculosis of larynx, trachea and bronchus, without mention of bacteriological or histological confirmation	1	0	0.0	21.0	100.0
257. A028 - Other specified salmonella infections	1	0	0.0	13.0	0.0
258. A064 - Amoebic liver abscess	1	0	0.0	7.0	0.0
259. A681 - Tick-borne relapsing fever	1	0	0.0	2.0	0.0
260. G008 - Other bacterial meningitis	1	1	100.0	2.0	0.0
261. A022 - Localized salmonella infections	1	0	0.0	13.0	0.0
262. I00X - Rheumatic fever without mention of heart involvement	1	0	0.0	18.0	0.0
263. K832 - Perforation of bile duct	1	0	0.0	13.0	0.0
264. A192 - Acute miliary tuberculosis, unspecified	1	0	0.0	16.0	0.0
265. O910 - Infection of nipple associated with childbirth	1	0	0.0	0.0	0.0
266. G01X - Meningitis in bacterial diseases classified elsewhere	1	0	0.0	154.0	0.0
267. A188 - Tuberculosis of other specified organs	1	0	0.0	9.0	0.0
268. A70X - Chlamydia psittaci infection	1	0	0.0	2.0	0.0
269. N761 - Subacute and chronic vaginitis	1	0	0.0	0.0	0.0
270. J168 - Pneumonia due to other specified infectious organisms	1	0	0.0	16.0	0.0

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DEFINING AND MEASURING SUSPICION OF SEPSIS: AN ANALYSIS OF ROUTINE DATA

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ABSTRACT

OBJECTIVES

To define the target population of patients who have suspicion of sepsis and to provide a basis for assessing the burden of suspicion of sepsis; and the evaluation of sepsis guidelines and improvement programmes.

DESIGN

Retrospective analysis of routinely collected hospital administrative data.

SETTING

Secondary care, eight NHS Acute Trusts.

PARTICIPANTS

Hospital Episode Statistics data for 2013-2014 was used to identify all admissions with a primary diagnosis listed in the "suspicion of sepsis" coding set. The suspicion of sepsis coding set consists of all bacterial infective diagnoses.

RESULTS

We identified 47475 admissions with suspicion of sepsis, equivalent to a rate of 17 admissions per 1000 adults in a given year. The mortality for this group was 7.2% during their acute hospital admission. Urinary tract infection was the most common diagnosis and lobar pneumonia was associated with the most deaths. A short list of ten diagnoses can account for 85% of the deaths.

CONCLUSIONS

Patients with suspicion of sepsis can be identified in routine administrative data. It is these patients who should be screened for sepsis and are the target of programmes to improve the detection and treatment of sepsis. The effectiveness of such programmes can be evaluated by examining the outcomes of patients with suspicion of sepsis.

KEY WORDS: sepsis, suspicion of sepsis, epidemiology, improvement programmes

STRENGTHS & LIMITATIONS OF THIS STUDY

- Our methodology for identifying suspicion of sepsis (SOS) uses routine administrative data, providing a means of assessing the SOS burden and comparing patient outcomes over time and across organisations.
- Monitoring the outcomes of SOS patients provides a simple and effective means of measuring the impact of sepsis improvement programmes.
- The analysis allowed the most common and the most high risk infections to be identified.
- The mortality figures are limited to in hospital deaths: 30 day mortality data was unavailable.
- The estimates for the SOS burden are based on Hospital Episode Statistics data which ultimately may not be as accurate as prospective data based on clinical and physiological measurements.

Sepsis, defined as a "life-threatening organ dysfunction caused by a dysregulated host response to infection",[1] is one of the leading causes of death.[2,3] The incidence of sepsis is thought to be increasing [4-7], with estimates of up to 300 cases per 100,000 population,[8] and it has been recently cited as the most expensive reason for hospitalisation in the US.[9] Rapid, evidence-based, aggressive treatment and assiduous review are vital for preserving post-recovery function and ensuring survival. Sepsis is most common in the elderly and those with impaired immune systems and is associated with reduced quality of life and high rates of late mortality in those who survive.[10,11]

Worldwide awareness of sepsis has been increasing due to high profile media attention, coupled with reports from the surviving sepsis campaign and a multitude of national regulators and expert bodies.[12-15] The early detection and treatment of sepsis has been highlighted as a major focus for improvement. For example, in the UK the identification and early treatment of sepsis is the target of a major national campaign and also the focus for Commissioning for Quality and Innovation (CQUIN) for 2015-2018, a financial incentive system.[16] The lack of suitable metrics for sepsis have hampered evaluation and some have suggested that until this is resolved no sepsis campaigns should be launched.[17]

Measures of the incidence of sepsis

There are three broad approaches to assessing the incidence of sepsis: through laboratory analytic tests such as blood cultures, through clinical judgement and through administrative databases (essentially the recording of clinical judgement). Many patients with sepsis do not have currently identifiable bacterial growth in blood tests (positive blood cultures), meaning that these investigations alone cannot assess the incidence of sepsis.[18,19] Clinical studies of sepsis have been primarily focused on intensive care units (ICUs) and suggest that the incidence of severe sepsis in intensive care is approximately 30%.[20,21] However, these studies, while informative in the intensive care environment, do not address the incidence of sepsis in other clinical settings within the hospital which is where most improvement programmes are now focused and where the majority of septic patients are managed.

The most practical means of assessing the incidence of sepsis in the wider hospital environment is through the analysis of administrative databases. However there is great variability in estimates of sepsis incidence depending on the coding set used [22,23] and changes in coding practices overtime make comparisons between years difficult.[17,22,24] In the UK,

clinicians rarely document "sepsis or septicaemia" in the admission documentation and tend to prioritise documenting the source of infection.[12,13] Official estimates for sepsis incidence, such as the Health Episode Statistic figures reported by NHS England, are broadly based on septicaemia codes,[5] and therefore underestimate the true incidence. Studies in the US frequently report rising sepsis incidence and falling mortality: it is unclear whether the falling mortality is due to actual improvements in care or a diluting effect of increased coding of patients who are less sick than those who would previously have been included.[25] In any case, the wider aim is not so much the treatment of sepsis as the prevention of sepsis through early intervention in patients who are at risk of sepsis.

Suspicion of sepsis

The concept of assessing and treating patients with suspected sepsis is central to the recently published National Institute for Health and Care Excellence (NICE) guidelines, with clinicians urged to think sepsis for all patients with signs of infection.[26,27] In practice clinicians do not wait to diagnose sepsis but rapidly treat patients with an infection that is serious enough to warrant hospital admission; they endeavour to intervene to prevent full blown sepsis developing and to interrupt the dangerous dysregulated and harmful immune response that may emerge. Some of these patients will of course already have a "bad or serious infection" that is sufficient to warrant the term sepsis. Most sepsis campaigns and improvement programmes do not actually target the treatment of fully developed sepsis but instead are aimed at the rapid detection and treatment of patients who have suspected sepsis when admitted to hospital from the community. This means that we must, first and foremost, identify those patients who either have early sepsis or who have an infection which might develop into sepsis if not properly treated.

The group, "suspicion of sepsis", consists primarily of patients who have a bacterial infection serious enough to require hospital admission.[28,29] Defining this group is essential to the implementation of NICE guidelines and to all the recommendations for research proposed in the guidelines.[26] Although there are non-bacterial causes of sepsis (e.g. viruses, protozoa), these are (generally) far less common and amenable to treatment. Given that the majority of septic patients have community-acquired infections,[30] our focus, and that of most sepsis improvement programmes, will be on patients with infections at the time of admission. To evaluate programmes aimed at early detection and intervention we must therefore define a "suspicion of sepsis" group and monitor the progress of its members. A successful

intervention would see a reduction in later sepsis (however measured) but even in the absence of reliable sepsis definition we could monitor mortality, length of stay and other indices of outcome in a suspicion of sepsis group.

Identifying patients with "suspicion of sepsis"

The primary aim of this study is to estimate the number of patients with suspicion of sepsis (SOS) on admission to hospital and their outcomes (mortality, length of stay, readmission rate). We focus on patients who either have bacterial infections which may lead to sepsis or which have already led to early sepsis. Analysis of a full list of ICD-10 diagnostic infection codes that can cause sepsis will provide clinical insight into which infections are the most frequent, which are the most dangerous and which might be prioritised for future improvement strategies. The full list of infection codes will inevitably include many rare or unusual diagnoses which would not be useful in assessing routine local activity or the impact of sepsis improvement programme. A secondary aim is therefore to propose a short pragmatic set of codes which can be used as a key aspect of a measurement suite for tracking the progress of sepsis improvement efforts in the UK.

METHOD

A list of International Statistical Classification of Diseases and Related Health Problems Tenth Revision (ICD-10: 2015) codes was developed for infective bacterial pathogens that can cause sepsis (see Appendix A). The coding set entitled "Suspicion of Sepsis" was established on the basis of clinical consensus: a consultant in acute medicine (MIK) reviewed the full list of ICD-10 codes and identified all codes known to be infective bacterial pathogens, requiring treatment with antibiotics. Specialist consultants for each organ system were then asked to verify the list of codes relevant to their speciality and the codes were subsequently adjusted based on their feedback. The list also includes specific sepsis codes (ICD-10 codes A40 and A41 and their derivatives) which are commonly used in the UK for instances of sepsis where the source of infection is unknown.[12 13]

Hospital Episode Statistics (HES) data was obtained for all acute trusts in the Oxford Academic Health Science Network (AHSN) region (n=8) for the financial year 2013-14: the region covers a population of 3.3 million. The data originated from the Health and Social

Care Information Centre (HSCIC). A data warehouse was created in Microsoft SQL Server for running queries and completing data analysis.

We analysed the admission episode to determine if any of the ICD-10 "Suspicion of Sepsis" codes appeared as the primary diagnosis. Coders use information from patient notes to restrospectively determine the primary reason for admission. Patients under the age of 18 were excluded. For each identified admission, the following information was determined: age at admission, sex, number of hospital deaths and associated mortality, length of stay (LOS) and readmission rate.[a] Population data provided by the Clinical Commissioning Groups (CCGs) which fall within the Oxford AHSN region was used to estimate a population incident rate.

Patient involvement

Patient experiences guided the principles of this study: a consistent theme in patient stories and local reviews of sepsis cases is that early symptoms were not recognised. Patients were not involved in the study design or the technical analysis of administrative databases. The concepts of the paper have been presented to both patients and carers in the context of measuring the impact of sepsis improvement programmes.

RESULTS

Incidence and demographics

In 2013-14, 47475 admissions were identified in the Oxford AHSN region using the "suspicion of sepsis" coding set, yielding a population estimate of 17 SOS hospital admissions per 1000 adults in a given year. The overall in-hospital mortality rate for this group was 7.2%, which represents 3440 deaths. The mean length of stay (LOS) was 9.2 days and 6.7% of SOS patients were readmitted within 30 days.

The number of SOS admissions by age and gender and the mortality rate by age are shown in Figure 1. There was no missing data.The patient was female in 52.8% of admissions. The number of admissions increased gradually with age, before decreasing for over 85s. Women between 18 and 35 (child-bearing age) were almost twice as likely as men of the same age to

[a] A patient was classified as a readmission if they were admitted as an emergency readmission between 1 and 30 days after their previous discharge. The main speciality of the two spells needed to match in order to be classified as a readmission.

have suspected sepsis and women over 85 also had a higher incidence than men, likely as a result of the higher female population in comparison to men over 85 years. For all other age groups, the number of SOS admissions in men and women were similar. Hospital mortality increased with age. The mortality rate was less than 1% for all age groups up to aged 45. From 46 upwards, the mortality increased exponentially: for patients over 85, the mortality was 19.2%.

Most common diagnoses

The following four ICD-10 chapters combined account for almost 85% of SOS admissions: "Diseases of the Respiratory System" (39.8%), "Diseases of the Digestive System" (11.1%), "Diseases of Genitourinary System" (21.0%) and "Diseases of Skin and Subcutaneous Tissue" (12.5%). 2577 (5.4%) of the SOS admissions had a sepsiscode (a code commencing A40 or A41) as their primary diagnosis.

Table 1 lists the twenty five most common diagnoses, alongside their respective mortality rates, number of deaths, LOS and readmission rates. A complete list of all the suspicion of sepsis diagnoses with the number of admissions, number of deaths, mortality, length of stay, and readmission rate is presented in Appendix B. The majority of the diagnoses in Table 1 are infections of the respiratory system. The most common diagnosis was urinary tract infection. A41.9 sepsis, the most common of the sepsis codes, was the seventhmost common SOS diagnosis.

The secondary aim of this study was to develop a short set of codes which could be easily tracked. The 25 diagnoses in Table 1 capture 80.3% of the total number of SOS admissions and 87.6% of the deaths. These 25 diagnoses include a number of diagnoses which are common but rarely lead to poor outcomes.

Diagnoses associated with the most deaths

The most important patients to identify and track in improvement programmes are those who have the poorest outcomes. Table 2 lists the ten diagnoses associated with the most deaths. Lobar pneumonia was associated with the most deaths, followed by pneumonia unspecified and then urinary tract infection. A41.9 sepsis was fourth on the list. Respiratory infections featured frequently in Table 1: indeed diagnoses from the ICD-10 chapter "Diseases of the Respiratory System" accounted for 69.8% of the total number of SOS deaths.

Together the ten diagnoses listed in Table 2 account for 87.3% of the total number of SOS deaths and 59.7% of the total number of SOS admissions. The mortality for this group of ten diagnoses is 10.6%, the mean LOS is 9.6 days and the readmission rate is 7.3%: these are much poorer outcomes than for the 25 more common diagnoses where the mortality is 7.9%, the mean LOS is 6.0 days and the mean readmission rate is 6.5%. Figure 2 shows a visual representation of these ten high risk diagnoses, their frequency, their outcomes (mortality and length of stay) and the type of infection. Early intervention and treatment improvement programmes should aim to improve the outcomes for patients admitted to hospital with these ten diagnoses.

DISCUSSION

Our methodology identifies those patients who should be routinely screened for sepsis on admission to hospital. Based on the identification of 47,475 suspicion of sepsis admissions in Oxford AHSN region in the financial year 2013-14, we estimate 17 SOS hospital admissions in a population of 1000 adults in a given year. Analysis of the individual SOS diagnoses allows a short pragmatic set of codes to be developed. For instance, the top ten diagnoses associated with the highest numbers of hospital deaths can account for 85% of the total number of SOS deaths: monitoring the outcomes of patients admitted to hospital with one of these ten crucial diagnoses, (e.g. mortality, length of stay, readmission rate), would be a pragmatic and effective means of assessing sepsis campaigns and improvement efforts.

Previous studies have found that the number of recorded septic episodes has artificially increased as a result of increased coding rather than solely more cases of sepsis, particularly in the US.[24] By tracking infective diagnoses, our methodology avoids this bias and hence would be a more effective measure of improvement over longer time periods. Clinical specialities are also more easily able to identify and track patients who are particularly relevant to them. Different countries could also use the methodology from this study to identify the most common and most fatal suspicion of sepsis diagnoses in their countries. The full suspicion of sepsis coding set could also be used to compare figures internationally for the population with suspicion of sepsis.

Future research and evaluation

We have been able to estimate the size of the suspicion of sepsis population on admission to hospital in our region; this should now be done nationally. Ideally we would also want to measure the percentage of SOS cases who develop definite sepsis, which would mean we would have a means of evaluating campaigns and programmes which aim to improve the detection and early treatment of potential sepsis. However, major improvements are needed in the quality of coding of sepsis if we are to use ICD codes to identify definite cases of sepsis. Even if we used case note review, evidence shows that diagnosing sepsis is subjective and variable.[31] The exact size of the sepsis "bubble" within the SOS set is likely to remain unknown in the absence of a definitive diagnostic test. However, linking the SOS database with electronic clinical observation data (e.g. physiology and pathology blood results) may allow specific definitions of sepsis to be applied. A potential surrogate measure may be the proportion of SOS patients admitted to intensive care.

Future studies can use the suspicion of sepsis population to study predictors of poor outcomes, for example by linking the SOS database with electronic clinical observation data. Suspicion of sepsis could also be used to assess the usefulness of potential biomarkers and to assess the impact of improvement campaigns, from small scale quality improvement work to national strategies such as the new NICE guidelines. Future studies should also estimate the costs and associated bed days for suspicion of sepsis.

Limitations

Our clinical assumption in reporting any-cause mortality for suspicion of sepsis diagnoses is that the presence of infection has a major impact on outcomes, above and beyond other factors such as comorbidities, but this ought to be tested. Furthermore, our mortality figures are based on Hospital Episode Statistics data and are therefore limited to in hospital deaths: future studies should also endeavour to assess 30 day mortality. Our estimates for the size of the SOS population are based on ICD codes which ultimately may not be as accurate as prospective data based on clinical and physiological measurements. However, our approach can be easily and cheaply used by any organisation to identify and monitor this critical group of patients. Our methodology measures suspicion of sepsis on admission; it does not address patients who develop an infection during their hospital stay. It is also worth noting that our estimates are based on one area of the country. Variability between regions is likely to be affected by such factors as social economic conditions, the quality of the hospitals and the

average age of the population. Our figures for the population incidence with suspicion of sepsis do suggest however that the national burden is substantial.

Conclusions

We propose that patients admitted to hospital for infection ("Suspicion of Sepsis") are a critical target population both for screening for sepsis and for monitoring the impact of sepsis improvement efforts. This group can be easily identified from routine administrative data. Analysis of local UK data yields an estimate of 17 hospital admissions with suspicion of sepsis per 1000 adults in a given year and revealed that a short list of ten diagnoses can capture 85% of suspicion of sepsis deaths. Monitoring the outcomes of suspicion of sepsis patients is a simple and effective measurement strategy for evaluating programmes aiming to improve the detection and treatment of sepsis.

TABLES

Table 1: **Top 25 most common "Suspicion of Sepsis" diagnoses in Oxford AHSN region (2013-14)**

Diagnosis	No. of admissions	No. of deaths	Mortality (%)	LOS	Readmission (%)
1. N39.0 - Urinary tract infection, site not specified	7088	285	4.0	9.0	6.4
2. J18.1 - Lobar pneumonia, unspecified	5265	990	18.8	9.8	6.3
3. J22.X - Unspecified acute lower respiratory infection	3808	167	4.4	6.5	7.4
4. J18.9 - Pneumonia, unspecified	3126	483	15.5	9.6	7.1
5. L03.1 - Cellulitis of other parts of limb	2983	62	2.1	6.9	7.5
6. J44.0 - Chronic obstructive pulmonary disease with acute lower respiratory infection	2854	184	6.4	7.2	11.3
7. A41.9 - Sepsis, unspecified	1882	280	14.9	9.2	10.7
8. T81.4 - Infection following a procedure, not elsewhere classified	1067	3	0.3	5.9	7.7
9. J03.9 - Acute tonsillitis, unspecified	1055	0	0.0	1.2	5.7
10. K35.8 - Acute appendicitis, other and unspecified	993	0	0.0	2.9	6.4
11. N12.X - Tubulo-interstitial nephritis, not specified as acute or chronic	809	1	0.1	3.5	3.5
12. K61.0 - Anal abscess	781	0	0.0	1.2	5.6
13. J69.0 - Pneumonitis due to food and vomit	776	260	33.5	14.1	5.0
14. L02.4 - Cutaneous abscess, furuncle and carbuncle of limb	710	0	0.0	2.5	5.6
15. L05.0 - Pilonidal cyst with abscess	533	0	0.0	0.6	4.9
16. L02.2 - Cutaneous abscess, furuncle and carbuncle of trunk	527	1	0.2	2.5	8.2
17. O23.4 - Unspecified infection of urinary tract in pregnancy	518	0	0.0	1.3	1.0
18. K80.0 - Calculus of gallbladder with acute cholecystitis	517	6	1.2	4.7	8.5
19. K37.X - Unspecified appendicitis	505	1	0.2	2.5	3.8
20. J18.0 - Bronchopneumonia, unspecified	432	242	56.0	10.5	5.8
21. J36.X - Peritonsillar abscess	429	0	0.0	1.3	2.8
22. N45.9 - Orchitis, epididymitis and epididymo-orchitis without abscess	413	0	0.0	1.8	6.1
23. A41.5 - Sepsis due to other Gram-negative organisms	360	40	11.1	11.5	10.8
24. T84.5 - Infection and inflammatory reaction due to internal joint prosthesis	345	4	1.2	19.1	5.5
25. K81.9 - Cholecystitis, unspecified	339	5	1.5	4.0	8.8
	***n* = 38115**	***n* = 3014**	***m* = 6.9**	***m* = 6.0**	***m* = 6.5**

Table 2: **Top ten "Suspicion of Sepsis" diagnoses associated with death in Oxford AHSN region (2013-14)**

Diagnosis	No. of Deaths	No. of admissions	Mortality (%)	LOS	Readmission (%)
1. J18.1 - Lobar pneumonia, unspecified	990	5265	18.8	9.8	6.3
2. J18.9 - Pneumonia, unspecified	483	3126	15.5	9.6	7.1
3. N39.0 - Urinary tract infection, site not specified	285	7088	4.0	9.0	6.4
4. A41.9 - Sepsis, unspecified	280	1882	14.9	9.2	10.7
5. J69.0 - Pneumonitis due to food and vomit	260	776	33.5	14.1	5.0
6. J18.0 - Bronchopneumonia, unspecified	242	432	56.0	10.5	5.8
7. J44.0 - Chronic obstructive pulmonary disease with acute lower respiratory infection	184	2854	6.4	7.2	11.3
8. J22.X - Unspecified acute lower respiratory infection	167	3808	4.4	6.5	7.4
9. L03.1 - Cellulitis of other parts of limb	62	2983	2.1	6.9	7.5
10. K63.1 - Perforation of intestine (nontraumatic)	51	136	37.5	13.0	5.9
	***n* = 3004**	***n* = 28350**	***m* = 19.3**	***m* = 9.6**	***m* = 7.3**

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Contributors: MIK conceived the study. IM carried out the analysis and BP prepared all tables and figures. BP and CV prepared the first draft of the paper. All authors provided critical feedback and contributions to the final paper.

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Competing interests: MIK reports grants for roles as clinical lead for sepsis across Oxford Academic Health Science Network and clinical lead of the Patient Safety Collaborative, Wessex. BP and IM declare no competing interests. CV declares grants from Oxford Academic Health Science Network, during the conduct of the study and occasional consultancy work on patient safety unrelated to this project.

Ethical approval: Not required as the data was routinely collected hospital administrative data and not in a patient identifiable format.

Data sharing: A full list of the suspicion of sepsis ICD-10 codes is given in Appendix A. Additional information on methodology can be obtained from the corresponding author on request. No additional data is available.

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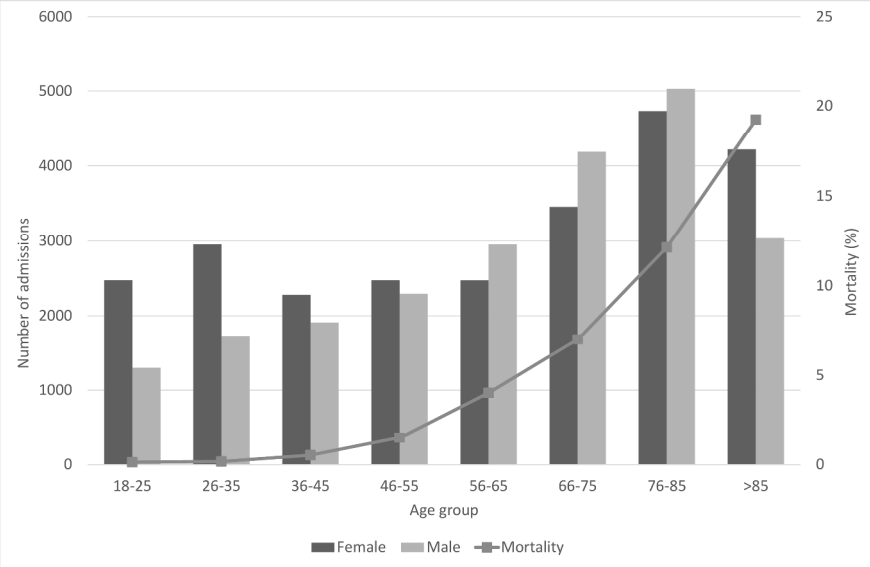

Figure 1: Suspicion of sepsis admissions and mortality by age and gender

297x209mm (300 x 300 DPI)

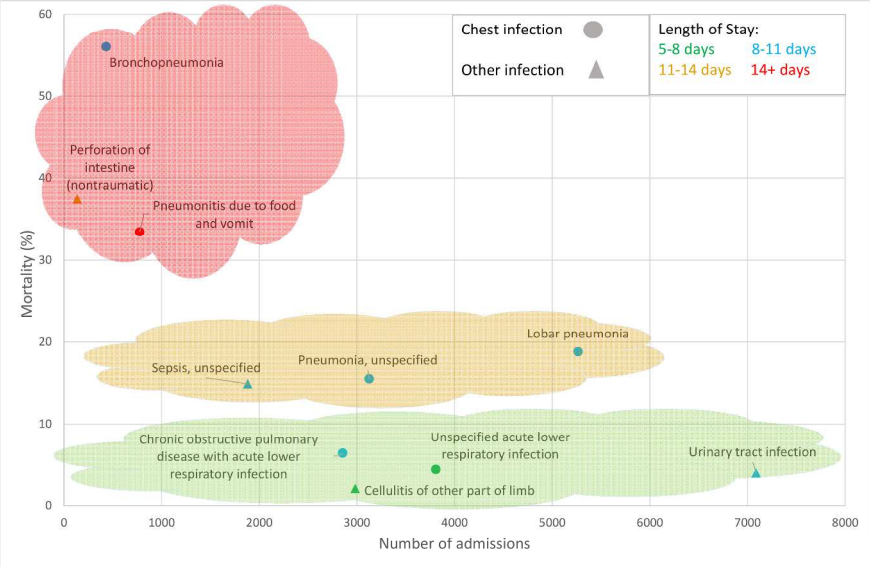

Figure 2: Top 10 suspicion of sepsis diagnoses associated with death

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APPENDIX A

"Suspicion of sepsis" coding set: ICD-10 bacterial infection codes

I. Certain Infectious and parasitic diseases

1. A01 Typhoid and paratyphoid fevers (incl. A01.0, A01.1, A01.2, A01.3, A01.4)
2. A02 Other salmonella infections (incl. A02.0, A02.1, A02.2, A02.8, A02.9)
3. A03 Shigellosis (incl. A03.0, A03.1, A03.2, A03.3, A03.8, A03.9)
4. A04 Other bacterial intestinal infections (incl. A04.0, A04.1, A04.2, A04.3, A04.4, A04.5, A04.6, A04.7, A04.8, A04.9)
5. A06 Amoebiasis (incl. A06.0, A06.1, A06.2, A06.3, A06.4, A06.5, A06.6, A06.7, A06.7, A06.8, A06.9)
6. A15 Respiratory tuberculosis (incl. A15.0, A15.2, A15.3, A15.4, A15.5, A15.6, A15.7, A15.8, A15.9)
7. A16 Respiratory tuberculosis, not confirmed bacteriologically or histologically (incl. A16.0, A16.1, A16.2, A16.3, A16.4, A16.5, A16.7, A16.8, A16.9)
8. A17 Tuberculosis of nervous system (incl. A17.0, A17.1, A17.8, A17.9)
9. A18 Tuberculosis of other organs (incl. A18.0, A18.1, A18.2, A18.3, A18.4, A18.5, A18.6, A18.7, A18.8)
10. A19 Miliary tuberculosis (incl. A19.0, A19.1, A19.2, A19.8, A19.9)
11. A27 Leptospirosis (incl. A27.0, A27.8, A27.9)
12. A32 Listerosis (incl. A32.0, A32.1, A32.7, A32.8, A32.9)
13. A37 Whopping cough (all subcategories)
14. A38 Scarlet fever
15. A39 Meningococcal infection (incl. A39.0, A39.1, A39.2, A39.4, A39.5, A39.8, A39.9)
16. A40 Streptococcal sepsis (incl. A40.0, A40.1, A40.2, A40.3, A40.8, A40.9)
17. A41 Other Sepsis (incl. A41.0, A41.1, A41.2, A41.3, A41.4, A41.5, A41.8, A41.9)
18. A42 Actinomycosis (all subcategories)
19. A43 Nocardiosis (all subcategories)
20. A44 Bartenollosis (all subcategories)
21. A46 Erysipelas
22. A48 Other Bacterial diseases, not elsewhere classified (incl. A48.0, A48.1, A48.2, A48.3, A48.4, A48.8)
23. A49 Bacterial infection of unspecified site (incl. A49.0, A49.1, A49.2, A49.3, A49.8, A49.8, A49.9)
24. A51 Early syphilis (all subcategories)
25. A54 Gonococcal infection (incl. A54.1, A54.2, A54.3, A54.4, A54.5, A54.6, A54.8, A54.9)
26. A55 Chlamydial lymhogranuloma (venereum)
27. A56 Other sexually transmitted chlamydial diseases (incl. A56.0, A56.1, A56.2, A56.3, A56.4, A56.8)
28. A68 Relapsing fevers (all subcategories)
29. A69.2 Lyme disease
30. A70 Chlamydia psittaci infection

31. A75 Typhus fever (all subcategories)
32. A77 Spotted fever (all subcategories)
33. A78 Q fever
34. A79 Other rickettsioses (all subcategories)
35. B59 Pneumocystosis

VI. Diseases of the nervous system

36. G00 Bacterial meningitis, not elsewhere classified (incl. G00.0, G00.1, G00.2, G00.3, G00.8, G00.9)
37. G01 Meningitis in bacterial diseases classified elsewhere
38. G04.2 Bacterial meningoencephalitis and meningomyelitis, not elsewhere classified
39. G06 Intracranial and intraspinal abscess and granuloma (incl. G06.0, G06.1, G06.2)

VIII. Diseases of the ear and mastoid process

40. H60 Otitis externa (incl. H60.0, H60.1, H60.2, H60.3)
41. H66 Suppurative and unspecified otitis media (incl. H66.0, H66.4, H66.9)
42. H67.0 Otitis media in bacterial diseases classified elsewhere
43. H68.0 eustachian salpingitis
44. H70 Mastoiditis and related conditions (incl. H70.0, H70.9)
45. H73.0 Acute myringitis

IX. Diseases of the circulatory system

46. I00 Rheumatic fever without mention of heart involvement
47. I01 Rheumatic fever with heart involvement (incl. I01.0, I01.1, I01.2, I01.8, I01.9)
48. I02 Rheumatic chorea (incl. I02.0, I02.9)
49. I33 Acute and subacute endocarditis (incl. I33.0, I33.9)
50. I38 Endocarditis, valve unspecified

X. Diseases of the respiratory system

51. J01 Acute sinusitis (incl. J01.0, J01.1, J01.2, J01.3, J01.4, J01.8, J01.9)
52. J02 Acute pharyngitis (incl. J02.0, J02.9)
53. J03 Acute tonsillitis (incl. J03.0, J03.9)
54. J05.1 Acute epiglottitis
55. J06.9 Acute upper respiratory infection, unspecified
56. J13 Pneumonia due to Streptococcus pneumoniae,
57. J14 Pneumonia due to Haemophilus influenza,
58. J15 Bacterial pneumonia, not elsewhere classified (J15.0, J15.1, J15.2, J15.3, J15.4, J15.5, J15.6, J15.7, J15.8, J15.9)
59. J16 Pneumonia due to other infectious organisms, not elsewhere classified (incl. J16.0, J16.8)]
60. J17.0 Pneumonia in bacterial diseases classified elsewhere (incl. J17.0, J17.8)
61. J18 Pneumonia, organism unspecified (including J18.0, J18.1, J18.2, J18.8 and J18.9)

62. J20 Acute bronchitis (incl. J20.0, J20.1, J20.2, J20.8, J20.9)
63. J22 Unspecified acute lower respiratory infection
64. J36 Peritonsillar abscess
65. J39 Other diseases of upper respiratory tract (incl. J39.0, J39.1)
66. J44.0 Chronic obstructive pulmonary disease with acute lower respiratory infection
67. J69 Pneumonitis due to solids and liquids (incl. J69.0, J69.8)
68. J84.9 Interstitial pulmonary disease unspecified (interstitial pneumonia NOS)
69. J85 Abscess of lung and mediastinum (incl. J85.1, J85.2, J85.3)
70. J86 Pyothorax (incl. J86.0, J86.9)
71. J95.0 Sepsis of tracheostomy stoma
72. J98.5 Diseases of mediastinum, not elsewhere classified- Mediastinitis

XI. Diseases of the digestives system (dental disorders omitted)

73. K22.3 Perforation of oesophagus
74. K35 Acute appendicitis (incl. K35.2, K35.3, K35.8)
75. K37 Unspecified appendicitis
76. K57 Diverticular disease of intestine (incl. K57.0, , K57.2, , K57.4, K57.8,)
77. K61 Abscess of anal and rectal regions (incl. K61.0, K61.1, K61.2, K61.3, 61.4)
78. K63.0 Abscess of intestine
79. K63.1 Perforation of intestine (nontraumatic)
80. K65.0 Acute peritonitis (incl. K65.0, K65.8, K65.9)
81. K67 Disorders of peritoneum in infectious diseases classified elsewhere (all subcategories)
82. K75.0 Abscess of liver
83. K80.0 Calculus of gallbladder with acute cholecystitis/cholangitis (incl.K80.0, K80.1, K80.3, K80.4,)
84. K81 Cholecystitis (incl. K81.0, K81.1, K81.8, K81.9)
85. K82.2 Perforation of gallbladder
86. K83.0 Cholangitis
87. K83.2 Perforation of bile duct

XII. Diseases of skin and subcutaneous tissue

88. L00 Staphylococcal scalded skin syndrome
89. L01 Impetigo (L01.0, L01.1)
90. L02 Cutaneous abscess, furuncle and carbuncle (incl. L02.0, L02.1, L02.2, L02.3, L02.4, L02.8, L02.9)
91. L03 Cellulitis (including L03.0, L03.1, L03.2, L03.3, L03.8 and L03.9)
92. L05.0 Pilonidal cyst with abscess
93. L08 Other local infections of skin and subcutaneous tissue (incl. L08.0, L08.8, L08.9)
94. L30.3 Infective dermatitis
95. L53.3 Erythema marginatum
96. L98.0 Pyogenic granuloma

XIII. Diseases of the musculoskeletal system and connective tissue

97. M00 Pyogenic arthritis (incl. M00.0, M00.1, M00.2, M00.8, M00.9)
98. M01 Direct infections of joint in infectious and parasitic diseases classified elsewhere (incl. M01.0, M01.1, M01.2, M01.3)
99. M46.2 Osteomyelitis of vertebra
100. M46.4 Discitis, unspecified
101. M65 Synovitis and tenosynovitis (incl. M65.0, M65.1)
102. M71.0 Abscess of bursa
103. M72.6 Necrotizing fasciitis
104. M86 Osteomyelitis

XIV. Diseases of genitourinary system

105. N10 Acute tubulo-interstitial nephritis
106. N11 Chronic tubulo-interstitial nephritis (incl. N11.0, N11.1, N11.8, N11.9)
107. N12 Tubulo-intestitial nephritis, not specified as acute or chronic
108. N13.6 Pyonephrosis
109. N15.1 Renal and perinephric abscess
110. N15.9 Renal tubulo-interstitial disease, unspecified
111. N30 Cystitis, unspecified (including N30.0, N30.8, N30.9)
112. N34.0 Urethral abscess
113. N39.0 Urinary tract infection, site not specified
114. N41.0 Acute prostatitis
115. N43.1 Infected hydrocele
116. N45 Orchitis and epididymitis (incl. N45.0, N45.9)
117. N48.2 Other disorders of penis (incl. N48.1, N48.2)
118. N49.9 Inflammatory disorder of unspecified male genital organ
119. N61 Inflammatory disorders of breast
120. N70 Salpingitis and oophoritis (incl N70.0, N70.9)
121. N71 Inflammatory disease of uterus, except cervix (incl. N71.0, N71.9)
122. N73 Other female pelvic inflammatory diseases (incl. N73.0, N73.1, N73.2, N73.4, N73.9)
123. N75.1 Abscess of Bartholin gland
124. N76 Other inflammation of vagina and vulva (incl. N76.0, N76.1, N76.3, N76.4, N76.8)

XV. Pregnancy, Childbirth and the puerperium

125. O08.0 Genital tract and pelvic infection following abortion and ectopic and molar pregnancy
126. O23 Infections of genitourinary tract in pregnancy (incl. O23.0, O23.1, O23.2, O23.3, O23.4, O23.5, O23.9)
127. O41.1 Infection of amniotic sac and membranes
128. 085 Puerperal sepsis

129. 086 Other puerperal infections (incl. O86.0, O86.1, O86.2, O86.3, O86.4, O86.8)
130. O88.3 Obstetric pyaemic and septic embolism
131. 091 Infections of breast associated with childbirth (incl. O91.0, O91.1)

XVI. Certain conditions originating in the perinatal period

132. P36 Bacterial sepsis of newborn (incl. P36.0, P36.1, P36.2, P36.3, P36.4, P36.5, P36.8, P36.9)
133. P39 Other infections specific to the perinatal period (incl. P39.0, P39.2, P39.3, P39.4, P39.8, P39.9)
134. P78 Other perinatal digestives system disorders (P78.0, P78.1,)
135. T814 Infection following a procedure, not elsewhere classified,
136. T845 Infection and inflammatory reaction due to internal joint prosthesis

XVIII. Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified

137. R57.2 Septic shock
138. R65 Systemic Inflammatory Response syndrome (incl. R65.0, R65.1, R65.9)

Note: Codes B95-98 were not considered since they should never be used in primary coding. http://apps.who.int/classifications/icd10/browse/2016/en#/B95-B98

APPENDIX B

Full table of "suspicion of sepsis" diagnoses: number of admissions, deaths, mortality, length of stay and readmission rate

Diagnosis	No. of admissions	No. of deaths	Mortality (%)	LOS	Readmissions (%)
1. N39.0 - Urinary tract infection, site not specified	7088	285	4.0	9.0	6.4
2. J18.1 - Lobar pneumonia, unspecified	5265	990	18.8	9.8	6.3
3. J22.X - Unspecified acute lower respiratory infection	3808	167	4.4	6.5	7.4
4. J18.9 - Pneumonia, unspecified	3126	483	15.5	9.6	7.1
5. L03.1 - Cellulitis of other parts of limb	2983	62	2.1	6.9	7.5
6. J44.0 - Chronic obstructive pulmonary disease with acute lower respiratory infection	2854	184	6.4	7.2	11.3
7. A41.9 - Sepsis, unspecified	1882	280	14.9	9.2	10.7
8. T81.4 - Infection following a procedure, not elsewhere classified	1067	3	0.3	5.9	7.7
9. J03.9 - Acute tonsillitis, unspecified	1055	0	0.0	1.2	5.7
10. K35.8 - Acute appendicitis, other and unspecified	993	0	0.0	2.9	6.4
11. N12.X - Tubulo-interstitial nephritis, not specified as acute or chronic	809	1	0.1	3.5	3.5
12. K61.0 - Anal abscess	781	0	0.0	1.2	5.6
13. J69.0 - Pneumonitis due to food and vomit	776	260	33.5	14.1	5.0
14. L02.4 - Cutaneous abscess, furuncle and carbuncle of limb	710	0	0.0	2.5	5.6
15. L05.0 - Pilonidal cyst with abscess	533	0	0.0	0.6	4.9
16. L02.2 - Cutaneous abscess, furuncle and carbuncle of trunk	527	1	0.2	2.5	8.2
17. O23.4 - Unspecified infection of urinary tract in pregnancy	518	0	0.0	1.3	1.0
18. K80.0 - Calculus of gallbladder with acute cholecystitis	517	6	1.2	4.7	8.5
19. K37.X - Unspecified appendicitis	505	1	0.2	2.5	3.8
20. J18.0 - Bronchopneumonia, unspecified	432	242	56.0	10.5	5.8
21. J36.X - Peritonsillar abscess	429	0	0.0	1.3	2.8
22. N45.9 - Orchitis, epididymitis and epididymo-orchitis without abscess	413	0	0.0	1.8	6.1
23. A41.5 - Sepsis due to other Gram-negative organisms	360	40	11.1	11.5	10.8

24. T84.5 - Infection and inflammatory reaction due to internal joint prosthesis	345	4	1.2	19.1	5.5
25. K81.9 - Cholecystitis, unspecified	339	5	1.5	4.0	8.8
26. K35.3 - Acute appendicitis with localized peritonitis	318	2	0.6	5.2	6.6
27. K81.0 - Acute cholecystitis	312	7	2.2	6.0	8.3
28. M86.9 - Osteomyelitis, unspecified	310	7	2.3	14.8	9.4
29. N30.9 - Cystitis, unspecified	291	0	0.0	0.6	1.0
30. L03.0 - Cellulitis of finger and toe	289	1	0.3	3.0	4.2
31. K83.0 - Cholangitis	240	18	7.5	9.5	4.6
32. K81.1 - Chronic cholecystitis	237	0	0.0	1.7	5.9
33. K57.2 - Diverticular disease of large intestine with perforation and abscess	231	20	8.7	12.5	8.7
34. N61.X - Inflammatory disorders of breast	231	0	0.0	1.1	7.8
35. A04.7 - Enterocolitis due to Clostridium difficile	208	20	9.6	16.1	11.1
36. O86.0 - Infection of obstetric surgical wound	202	0	0.0	2.0	0.0
37. J06.9 - Acute upper respiratory infection, unspecified	190	1	0.5	1.1	7.9
38. L02.3 - Cutaneous abscess, furuncle and carbuncle of buttock	189	0	0.0	1.3	8.5
39. N73.9 - Female pelvic inflammatory disease, unspecified	180	0	0.0	2.9	7.8
40. J02.9 - Acute pharyngitis, unspecified	169	0	0.0	0.9	7.7
41. L08.9 - Local infection of skin and subcutaneous tissue, unspecified	165	1	0.6	3.8	4.8
42. N75.1 - Abscess of Bartholin's gland	159	0	0.0	0.8	2.5
43. M00.9 - Pyogenic arthritis, unspecified	140	5	3.6	11.9	6.4
44. A04.5 - Campylobacter enteritis	136	3	2.2	6.6	2.2
45. K80.3 - Calculus of bile duct with cholangitis	136	7	5.1	10.6	2.9
46. K63.1 - Perforation of intestine (nontraumatic)	136	51	37.5	13.0	5.9
47. L03.3 - Cellulitis of trunk	127	0	0.0	5.2	7.1
48. L03.2 - Cellulitis of face	124	0	0.0	3.2	1.6
49. K80.4 - Calculus of bile duct with cholecystitis	117	2	1.7	6.8	9.4
50. J86.9 - Pyothorax without fistula	114	7	6.1	13.0	8.8
51. H66.9 - Otitis media, unspecified	113	0	0.0	1.6	0.9
52. J13.X - Pneumonia due to Streptococcus pneumoniae	112	11	9.8	11.0	2.7
53. N30.8 - Other cystitis	109	0	0.0	0.9	0.9

54. N10.X - Acute tubulo-interstitial nephritis	108	1	0.9	4.0	4.6
55. O85.X - Puerperal sepsis	107	0	0.0	2.8	1.9
56. M86.6 - Other chronic osteomyelitis	103	0	0.0	12.7	4.9
57. K65.0 - Acute peritonitis	96	13	13.5	12.6	14.6
58. N13.6 - Pyonephrosis	93	6	6.5	14.8	5.4
59. I33.0 - Acute and subacute infective endocarditis	89	11	12.4	21.3	9.0
60. A41.8 - Other specified sepsis	87	32	36.8	10.5	9.2
61. A04.8 - Other specified bacterial intestinal infections	82	1	1.2	1.2	2.4
62. J84.9 - Interstitial pulmonary disease, unspecified	80	9	11.3	5.2	3.8
63. L98.0 - Pyogenic granuloma	80	0	0.0	0.1	3.8
64. K61.3 - Ischiorectal abscess	80	0	0.0	3.4	10.0
65. N76.4 - Abscess of vulva	73	0	0.0	1.4	4.1
66. A41.0 - Sepsis due to Staphylococcus aureus	70	24	34.3	17.7	1.4
67. O23.0 - Infections of kidney in pregnancy	66	0	0.0	2.9	0.0
68. M46.4 - Discitis, unspecified	65	1	1.5	17.9	4.6
69. M86.4 - Chronic osteomyelitis with draining sinus	65	0	0.0	15.4	1.5
70. O86.4 - Pyrexia of unknown origin following delivery	61	0	0.0	2.5	0.0
71. L02.1 - Cutaneous abscess, furuncle and carbuncle of neck	60	0	0.0	3.1	1.7
72. O23.5 - Infections of the genital tract in pregnancy	59	0	0.0	0.7	0.0
73. N71.9 - Inflammatory disease of uterus, unspecified	57	1	1.8	2.5	1.8
74. J20.9 - Acute bronchitis, unspecified	52	0	0.0	2.7	1.9
75. K65.9 - Peritonitis, unspecified	52	18	34.6	6.2	1.9
76. J15.1 - Pneumonia due to Pseudomonas	51	14	27.5	17.9	7.8
77. N70.9 - Salpingitis and oophoritis, unspecified	48	0	0.0	5.3	0.0
78. K75.0 - Abscess of liver	46	2	4.3	13.6	6.5
79. N41.0 - Acute prostatitis	45	0	0.0	0.8	0.0
80. M65.1 - Other infective (teno)synovitis	44	0	0.0	7.0	4.5
81. A49.8 - Other bacterial infections of unspecified site	44	4	9.1	11.6	13.6
82. L03.9 - Cellulitis, unspecified	44	3	6.8	6.1	11.4
83. O41.1 - Infection of amniotic sac and membranes	42	0	0.0	6.2	0.0
84. M00.0 - Staphylococcal arthritis and polyarthritis	41	1	2.4	14.8	2.4

85. A41.1 - Sepsis due to other specified staphylococcus	40	9	22.5	11.1	12.5
86. K57.1 - Diverticular disease of small intestine without perforation or abscess	39	0	0.0	1.4	2.6
87. N11.9 - Chronic tubulo-interstitial nephritis, unspecified	38	0	0.0	3.9	2.6
88. O86.2 - Urinary tract infection following delivery	38	0	0.0	1.6	0.0
89. M72.6 - Necrotizing fasciitis	38	11	28.9	20.4	2.6
90. N48.1 - Balanoposthitis	38	0	0.0	0.3	2.6
91. J01.9 - Acute sinusitis, unspecified	37	0	0.0	1.0	2.7
92. M86.8 - Other osteomyelitis	35	0	0.0	1.5	2.9
93. H60.1 - Cellulitis of external ear	35	0	0.0	2.4	0.0
94. A49.0 - Staphylococcal infection, unspecified site	34	5	14.7	14.5	8.8
95. A40.8 - Other streptococcal sepsis	34	6	17.6	16.1	5.9
96. L02.0 - Cutaneous abscess, furuncle and carbuncle of face	34	0	0.0	1.9	0.0
97. J05.1 - Acute epiglottitis	32	1	3.1	3.4	3.1
98. J14.X - Pneumonia due to Haemophilus influenzae	32	3	9.4	9.1	3.1
99. N48.2 - Other inflammatory disorders of penis	30	0	0.0	2.4	3.3
100. N45.0 - Orchitis, epididymitis and epididymo-orchitis with abscess	29	0	0.0	4.4	0.0
101. O91.1 - Abscess of breast associated with childbirth	29	0	0.0	2.0	17.2
102. M86.1 - Other acute osteomyelitis	28	0	0.0	16.1	7.1
103. J15.0 - Pneumonia due to Klebsiella pneumoniae	27	8	29.6	15.6	7.4
104. H60.2 - Malignant otitis externa	27	0	0.0	20.3	3.7
105. J39.0 - Retropharyngeal and parapharyngeal abscess	26	0	0.0	6.0	3.8
106. J86.0 - Pyothorax with fistula	26	0	0.0	13.9	3.8
107. A46.X - Erysipelas	25	0	0.0	1.7	0.0
108. L03.8 - Cellulitis of other sites	25	0	0.0	3.7	4.0
109. L30.3 - Infective dermatitis	23	0	0.0	3.5	13.0
110. J95.0 - Tracheostomy malfunction	23	1	4.3	5.1	21.7
111. G06.0 - Intracranial abscess and granuloma	22	1	4.5	22.6	0.0
112. N30.0 - Acute cystitis	22	0	0.0	3.0	4.5
113. R57.2 - Septic shock	21	11	52.4	11.2	9.5
114. A40.9 - Streptococcal sepsis, unspecified	21	3	14.3	14.9	9.5
115. A16.9 - Respiratory tuberculosis	20	1	5.0	6.8	5.0

unspecified, without mention of bacteriological or histological confirmation					
116. G00.9 - Bacterial meningitis, unspecified	20	2	10.0	12.1	0.0
117. A49.9 - Bacterial infection, unspecified	19	3	15.8	8.7	10.5
118. A40.0 - Sepsis due to streptococcus, group A	19	4	21.1	11.6	0.0
119. J15.4 - Pneumonia due to other streptococci	19	4	21.1	11.1	0.0
120. O23.1 - Infections of bladder in pregnancy	19	0	0.0	1.7	5.3
121. A41.2 - Sepsis due to unspecified staphylococcus	19	4	21.1	16.8	21.1
122. N15.1 - Renal and perinephric abscess	19	1	5.3	11.3	5.3
123. J20.8 - Acute bronchitis due to other specified organisms	19	0	0.0	3.0	0.0
124. H60.0 - Abscess of external ear	18	0	0.0	1.3	11.1
125. J15.2 - Pneumonia due to staphylococcus	18	5	27.8	19.7	11.1
126. A18.0 - Tuberculosis of bones and joints	18	0	0.0	9.4	11.1
127. M00.2 - Other streptococcal arthritis and polyarthritis	18	0	0.0	14.2	11.1
128. H70.9 - Mastoiditis, unspecified	18	0	0.0	3.1	5.6
129. A49.1 - Streptococcal infection, unspecified site	17	1	5.9	11.5	5.9
130. J69.8 - Pneumonitis due to other solids and liquids	17	5	29.4	12.2	5.9
131. A40.3 - Sepsis due to Streptococcus pneumoniae	16	2	12.5	10.7	0.0
132. O86.1 - Other infection of genital tract following delivery	16	0	0.0	2.2	0.0
133. A16.2 - Tuberculosis of lung, without mention of bacteriological or histological confirmation	16	2	12.5	8.9	0.0
134. A02.0 - Salmonella enteritis	15	0	0.0	7.0	6.7
135. G06.1 - Intraspinal abscess and granuloma	15	0	0.0	48.1	13.3
136. K65.8 - Other peritonitis	15	3	20.0	8.1	6.7
137. L08.8 - Other specified local infections of skin and subcutaneous tissue	15	0	0.0	6.4	0.0
138. A48.1 - Legionnaires' disease	14	0	0.0	12.5	0.0
139. B59.X - Pneumocystosis	14	5	35.7	15.6	21.4
140. N11.1 - Chronic obstructive pyelonephritis	14	0	0.0	4.2	0.0
141. K22.3 - Perforation of oesophagus	14	2	14.3	16.4	7.1

142. G00.1 - Pneumococcal meningitis	14	0	0.0	12.9	7.1
143. M00.8 - Arthritis and polyarthritis due to other specified bacterial agents	14	0	0.0	25.6	0.0
144. J98.5 - Diseases of mediastinum, not elsewhere classified	14	1	7.1	7.1	7.1
145. K61.1 - Rectal abscess	13	1	7.7	9.1	0.0
146. M65.0 - Abscess of tendon sheath	13	0	0.0	4.2	0.0
147. A40.1 - Sepsis due to streptococcus, group B	12	1	8.3	20.2	0.0
148. O08.0 - Genital tract and pelvic infection following abortion and ectopic and molar pregnancy	12	0	0.0	1.9	16.7
149. K63.0 - Abscess of intestine	12	0	0.0	9.3	16.7
150. O23.3 - Infections of other parts of urinary tract in pregnancy	11	0	0.0	1.9	18.2
151. A01.0 - Typhoid fever	11	0	0.0	7.9	9.1
152. H60.3 - Other infective otitis externa	10	0	0.0	2.2	30.0
153. A15.0 - Tuberculosis of lung, confirmed by sputum microscopy with or without culture	10	1	10.0	5.8	0.0
154. J85.1 - Abscess of lung with pneumonia	10	0	0.0	16.4	10.0
155. J18.8 - Other pneumonia, organism unspecified	10	0	0.0	2.5	0.0
156. J15.8 - Other bacterial pneumonia	9	1	11.1	15.2	0.0
157. A04.9 - Bacterial intestinal infection, unspecified	9	0	0.0	10.4	11.1
158. K57.4 - Diverticular disease of both small and large intestine with perforation and abscess	9	1	11.1	20.3	0.0
159. K82.2 - Perforation of gallbladder	9	0	0.0	22.7	11.1
160. N76.8 - Other specified inflammation of vagina and vulva	9	0	0.0	0.3	0.0
161. M46.2 - Osteomyelitis of vertebra	9	0	0.0	29.7	0.0
162. J85.2 - Abscess of lung without pneumonia	9	1	11.1	8.3	22.2
163. J39.1 - Other abscess of pharynx	8	0	0.0	4.6	0.0
164. A18.2 - Tuberculous peripheral lymphadenopathy	8	0	0.0	0.1	12.5
165. N76.0 - Acute vaginitis	8	0	0.0	2.4	0.0
166. L02.8 - Cutaneous abscess, furuncle and carbuncle of other sites	8	0	0.0	3.1	0.0
167. A41.4 - Sepsis due to anaerobes	8	0	0.0	12.9	12.5
168. L02.9 - Cutaneous abscess, furuncle and carbuncle, unspecified	8	0	0.0	0.5	0.0

169. A16.5 - Tuberculous pleurisy, without mention of bacteriological or histological confirmation	8	0	0.0	6.6	0.0
170. A40.2 - Sepsis due to streptococcus, group D	8	0	0.0	12.1	0.0
171. K57.0 - Diverticular disease of small intestine with perforation and abscess	8	2	25.0	11.1	0.0
172. J15.5 - Pneumonia due to Escherichia coli	8	2	25.0	10.4	0.0
173. K61.2 - Anorectal abscess	8	0	0.0	0.5	0.0
174. N11.0 - Nonobstructive reflux-associated chronic pyelonephritis	8	0	0.0	3.1	0.0
175. O86.8 - Other specified puerperal infections	8	0	0.0	1.9	0.0
176. K61.4 - Intrasphincteric abscess	7	0	0.0	2.0	0.0
177. M01.1 - Tuberculous arthritis	7	0	0.0	9.6	28.6
178. A69.2 - Lyme disease	7	0	0.0	29.6	14.3
179. G00.2 - Streptococcal meningitis	6	1	16.7	12.5	0.0
180. A39.0 - Meningococcal meningitis	6	0	0.0	9.3	0.0
181. I33.9 - Acute endocarditis, unspecified	6	0	0.0	22.3	0.0
182. A39.4 - Meningococcaemia, unspecified	6	0	0.0	8.2	16.7
183. J15.6 - Pneumonia due to other aerobic Gram-negative bacteria	6	0	0.0	13.0	0.0
184. J01.0 - Acute maxillary sinusitis	6	0	0.0	2.5	0.0
185. O23.9 - Other and unspecified genitourinary tract infection in pregnancy	6	0	0.0	0.5	0.0
186. H66.0 - Acute suppurative otitis media	6	0	0.0	3.5	0.0
187. J15.9 - Bacterial pneumonia, unspecified	6	0	0.0	3.0	16.7
188. K81.8 - Other cholecystitis	6	0	0.0	2.7	0.0
189. A04.4 - Other intestinal Escherichia coli infections	6	0	0.0	8.8	0.0
190. M71.0 - Abscess of bursa	6	0	0.0	1.8	0.0
191. M86.3 - Chronic multifocal osteomyelitis	6	0	0.0	0.0	0.0
192. A15.2 - Tuberculosis of lung, confirmed histologically	6	0	0.0	11.7	16.7
193. N34.0 - Urethral abscess	6	0	0.0	1.3	0.0
194. L01.0 - Impetigo [any organism] [any site]	5	0	0.0	2.2	20.0
195. A19.9 - Miliary tuberculosis, unspecified	5	2	40.0	29.0	20.0
196. H66.4 - Suppurative otitis media, unspecified	5	0	0.0	1.0	0.0

197. A37.9 - Whooping cough, unspecified	5	0	0.0	1.8	0.0
198. A18.3 - Tuberculosis of intestines, peritoneum and mesenteric glands	5	0	0.0	25.6	20.0
199. A15.6 - Tuberculous pleurisy, confirmed bacteriologically and histologically	5	1	20.0	18.4	0.0
200. A42.8 - Other forms of actinomycosis	5	0	0.0	6.8	0.0
201. N71.0 - Acute inflammatory disease of uterus	5	0	0.0	0.6	0.0
202. A03.9 - Shigellosis, unspecified	4	0	0.0	5.8	0.0
203. A17.0 - Tuberculous meningitis	4	0	0.0	41.5	0.0
204. G06.2 - Extradural and subdural abscess, unspecified	4	1	25.0	39.0	0.0
205. A17.8 - Other tuberculosis of nervous system	4	1	25.0	16.3	0.0
206. H70.0 - Acute mastoiditis	4	0	0.0	2.0	0.0
207. J02.0 - Streptococcal pharyngitis	4	0	0.0	2.3	25.0
208. A56.1 - Chlamydial infection of pelviperitoneum and other genitourinary organs	4	0	0.0	2.5	0.0
209. A39.8 - Other meningococcal infections	4	0	0.0	31.0	0.0
210. J03.0 - Streptococcal tonsillitis	3	0	0.0	1.7	0.0
211. A18.4 - Tuberculosis of skin and subcutaneous tissue	3	0	0.0	4.3	0.0
212. J01.8 - Other acute sinusitis	3	0	0.0	1.0	0.0
213. G04.2 - Bacterial meningoencephalitis and meningomyelitis, not elsewhere classified	3	1	33.3	14.3	0.0
214. A19.1 - Acute miliary tuberculosis of multiple sites	3	0	0.0	12.0	0.0
215. N43.1 - Infected hydrocele	3	0	0.0	2.7	0.0
216. N15.9 - Renal tubulo-interstitial disease, unspecified	3	0	0.0	2.3	0.0
217. N73.0 - Acute parametritis and pelvic cellulitis	3	0	0.0	4.7	0.0
218. A18.1 - Tuberculosis of genitourinary system	3	0	0.0	0.7	33.3
219. N70.0 - Acute salpingitis and oophoritis	3	0	0.0	5.0	0.0
220. A01.1 - Paratyphoid fever A	3	0	0.0	6.7	0.0
221. N11.8 - Other chronic tubulo-interstitial nephritis	2	0	0.0	9.0	0.0
222. A19.0 - Acute miliary tuberculosis of a single specified site	2	0	0.0	33.5	50.0
223. A27.0 - Leptospirosis icterohaemorrhagica	2	0	0.0	0.0	50.0

224. A15.3 - Tuberculosis of lung, confirmed by unspecified means	2	0	0.0	10.0	0.0
225. M86.0 - Acute haematogenous osteomyelitis	2	0	0.0	10.0	0.0
226. A48.3 - Toxic shock syndrome	2	0	0.0	10.5	0.0
227. A27.9 - Leptospirosis, unspecified	2	0	0.0	4.5	0.0
228. J15.7 - Pneumonia due to Mycoplasma pneumoniae	2	0	0.0	9.0	0.0
229. A02.9 - Salmonella infection, unspecified	2	0	0.0	5.0	0.0
230. N73.1 - Chronic parametritis and pelvic cellulitis	2	0	0.0	3.0	0.0
231. L01.1 - Impetiginization of other dermatoses	2	0	0.0	2.0	0.0
232. A32.7 - Listerial sepsis	2	0	0.0	17.0	50.0
233. A02.1 - Salmonella sepsis	2	0	0.0	10.5	50.0
234. J01.2 - Acute ethmoidal sinusitis	2	0	0.0	6.0	0.0
235. A32.1 - Listerial meningitis and meningoencephalitis	2	0	0.0	25.0	0.0
236. J01.1 - Acute frontal sinusitis	2	0	0.0	1.0	0.0
237. O86.3 - Other genitourinary tract infections following delivery	2	0	0.0	1.5	0.0
238. A32.9 - Listeriosis, unspecified	2	0	0.0	20.5	0.0
239. N76.3 - Subacute and chronic vulvitis	2	0	0.0	0.0	0.0
240. A03.3 - Shigellosis due to Shigella sonnei	2	0	0.0	4.0	0.0
241. A41.3 - Sepsis due to Haemophilus influenzae	1	0	0.0	18.0	0.0
242. A42.0 - Pulmonary actinomycosis	1	0	0.0	21.0	0.0
243. H73.0 - Acute myringitis	1	0	0.0	0.0	0.0
244. J15.3 - Pneumonia due to streptococcus, group B	1	0	0.0	84.0	0.0
245. A15.7 - Primary respiratory tuberculosis, confirmed bacteriologically and histologically	1	0	0.0	0.0	100.0
246. A17.1 - Meningeal tuberculoma	1	0	0.0	5.0	0.0
247. L08.0 - Pyoderma	1	0	0.0	3.0	0.0
248. A15.9 - Respiratory tuberculosis unspecified, confirmed bacteriologically and histologically	1	0	0.0	9.0	0.0
249. N49.9 - Inflammatory disorder of unspecified male genital organ	1	0	0.0	1.0	0.0
250. J18.2 - Hypostatic pneumonia, unspecified	1	0	0.0	7.0	0.0
251. M86.5 - Other chronic haematogenous osteomyelitis	1	0	0.0	13.0	0.0
252. A42.2 - Cervicofacial actinomycosis	1	0	0.0	0.0	0.0

253. A16.4 - Tuberculosis of larynx, trachea and bronchus, without mention of bacteriological or histological confirmation	1	0	0.0	21.0	100.0
254. A02.8 - Other specified salmonella infections	1	0	0.0	13.0	0.0
255. A06.4 - Amoebic liver abscess	1	0	0.0	7.0	0.0
256. A68.1 - Tick-borne relapsing fever	1	0	0.0	2.0	0.0
257. G00.8 - Other bacterial meningitis	1	1	100.0	2.0	0.0
258. A02.2 - Localized salmonella infections	1	0	0.0	13.0	0.0
259. I00.X - Rheumatic fever without mention of heart involvement	1	0	0.0	18.0	0.0
260. K83.2 - Perforation of bile duct	1	0	0.0	13.0	0.0
261. A19.2 - Acute miliary tuberculosis, unspecified	1	0	0.0	16.0	0.0
262. O91.0 - Infection of nipple associated with childbirth	1	0	0.0	0.0	0.0
263. G01.X - Meningitis in bacterial diseases classified elsewhere	1	0	0.0	154.0	0.0
264. A18.8 - Tuberculosis of other specified organs	1	0	0.0	9.0	0.0
265. A70.X - Chlamydia psittaci infection	1	0	0.0	2.0	0.0
266. N76.1 - Subacute and chronic vaginitis	1	0	0.0	0.0	0.0
267. J16.8 - Pneumonia due to other specified infectious organisms	1	0	0.0	16.0	0.0

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page no.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1 & 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6-7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-7*
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7-9
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	N/A
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7-8
		(b) Indicate number of participants with missing data for each variable of interest	7
		(c) Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	7-9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7

		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.